Harris
232880

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=> fil medl,caplus,biosis,embase,wpids;s prostate cancer and (oligonucleotide
or polynucleotide) and (pcr or polymerase chain react?)

COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.45       0.45

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L1           27 FILE MEDLINE
L2           32 FILE CAPLUS
L3           18 FILE BIOSIS
L4           21 FILE EMBASE
L5           27 FILE WPIDS

TOTAL FOR ALL FILES
L6          125 PROSTATE CANCER AND (OLIGONUCLEOTIDE OR POLYNUCLEOTIDE) AND
                (PCR OR POLYMERASE CHAIN REACT?)

=> s prostate (w)(tumor or tumour)(w)protein and hydrid? and l6

L7            0 FILE MEDLINE
L8            0 FILE CAPLUS
L9            0 FILE BIOSIS
L10           0 FILE EMBASE
L11           0 FILE WPIDS

TOTAL FOR ALL FILES
L12           0 PROSTATE (W)(TUMOR OR TUMOUR)(W) PROTEIN AND HYDRID? AND L6

=> s prostate (w)(tumor or tumour)(w)protein and  l6

L13           0 FILE MEDLINE
L14           0 FILE CAPLUS
L15           0 FILE BIOSIS
L16           0 FILE EMBASE
L17           1 FILE WPIDS

TOTAL FOR ALL FILES
L18           1 PROSTATE (W)(TUMOR OR TUMOUR)(W) PROTEIN AND L6

=> d;s l6 and hybrid?


L18  ANSWER 1 OF 1  WPIDS COPYRIGHT 2000   DERWENT INFORMATION LTD
AN   2000-171268 [15]   WPIDS
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DNN N2000-127248 DNC C2000-053337
TI New polypeptide useful for treating and diagnosing **prostate cancer** comprises an immunogenic portion of **prostate tumor protein.**
DC B04 D16 S03
IN DILLON, D C; HARLOCKER, S L; MITCHAM, J L; XU, J; YUQIU, J
PA (CORI-N) CORIXA CORP
CYC 85
PI WO 2000004149 A2 20000127 (200015)* EN 263p C12N015-12
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL QA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW
ADT WO 2000004149 A2 WO 1999-US15838 19990714
PRAI US 1999-288946 19990409; US 1998-115453 19980714; US 1998-116134 19980714; US 1998-159812 19980923; US 1998-159822 19980923; US 1999-232149 19990115; US 1999-232880 19990115
IC ICM C12N015-12
ICS A61K039-395; C07K014-47; C07K016-30; C12N005-02; C12N015-62; C12Q001-68; G01N033-574; G01N033-68
ICA A61P035-00

L19 9 FILE MEDLINE
L20 19 FILE CAPLUS
L21 6 FILE BIOSIS
L22 7 FILE EMBASE
L23 26 FILE WPIDS

TOTAL FOR ALL FILES
L24 67 L6 AND HYBRID?

=> s l24 not l18

L25 9 FILE MEDLINE
L26 19 FILE CAPLUS
L27 6 FILE BIOSIS
L28 7 FILE EMBASE
L29 25 FILE WPIDS

TOTAL FOR ALL FILES
L30 66 L24 NOT L18

=> dup rem l30

PROCESSING COMPLETED FOR L30
L31 48 DUP REM L30 (18 DUPLICATES REMOVED)

=> d 1-48 cbib abs;s xu j?/au,in;s dillon d?/au,in;s mitcham j?/au,in

L31 ANSWER 1 OF 48 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 2000-182420 [16] WPIDS
AB WO 200004150 A UPAB: 20000330
NOVELTY - Human presenilin-associated protein (HPAP-1; (I)), comprising the 180 amino acid sequence given in the specification and its fragment or
variants (with at least 90 % identity), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a **polynucleotide** (II) encoding (I), comprising the 819 bp sequence given in the specification;

(2) a **polynucleotide** which **hybridizes** to, is complementary to, or has at least 90% identity to (II);

(3) an expression vector comprising at least a fragment of (II);

(4) a host cell comprising the expression vector of (3);

(5) producing (I), comprising culturing the host cell of (4) and recovering (I) from the culture;

(6) a purified antibody which specifically binds (I);

(7) a purified agonist and/or antagonist of (I);

(8) treating or preventing disorder associated with decreased expression or activity of HPAP, comprising administering a pharmaceutical comprising (I);

(9) treating or preventing disorder associated with increased expression or activity of HPAP, comprising administering the antagonist of (12);

(10) detecting a **polynucleotide** comprising **hybridizing** the complementary **polynucleotide** of (2) to at least 1 of the nucleic acids in a sample, and detecting the **hybridization** complex formed (optionally, the nucleic acids in the sample are amplified by **PCR** prior to detection).

ACTIVITY - Cytostatic; antianemic; nootropic; neuroprotective; antiallergic; immunomodulatory; antianemic; antiarrhthymic; antiasthmatic; antiinflammatory; cardiant; hepatotropic; antidepresant; antidiabetic; antidiarrhoeal; anticonvulsant; nephrotropic; antigout; antithyroid; thyrominetic; hypotensive; gynecological; antiemetic; neuroleptic; thrombolytic; tranquilizer; vulnerary; antiulcer; ophthalmological; antiparkinsonian.

MECHANISM OF ACTION - Gene therapy.

USE - Human presenilin-associated protein (HPAP-1) encoding **polynucleotides**, polypeptides, agonists, antagonists and antibodies are used for in the diagnosis, treatment and prevention of neurological disorders (e.g. akathesia, Alzheimer's disease, amnesia, amyotrophic lateral sclerosis, bipolar disorder, catatonia, cerebral neoplasms, dementia, depression, diabetic neuropathy, Down's syndrome, tardive dyskinesia, dystonias, epilepsy, Huntington's disease, peripheral neuropathy, multiple sclerosis neurofibromatosis, Parkinson's disease, paranoid psychoses, post-therpetic neuralgia, schizophrenia and Tourette's disorder); cancers (e.g. adenocarcinoma, leukemia, melanoma, myeloma, sarcoma, teratocarcinoma and cancers of various organs); immune disorders (e.g. AIDS, Addison's disease, adult respiratory distress syndrome, allergies, ankylosing spondylitis, amyloidosis, anemia, asthma, atherosclerosis, autoimmune hemolytic anemia, autoimmune thyroiditis, bronchitis, cholecystitis, contact dermatitis, Crohn's disease, atopic dermatitis, dermatomyositis, diabetes mellitus, emphysema, episodic lymphopenia with lymphocytotoxins, erythroblastosis fetalis, erythema nodosum, atrophic gastritis, glomerulonephritis, Goodpasture's syndrome, gout, Grave's disease, Hashimoto's thyroiditis, hypereosinophilia, irritable bowel syndrome, multiple sclerosis, myasthenia gravis, myocardial or pericardial inflammation, osteoarthritis, osteoporosis, pancreatis, polymyositis, psoriasis, Reiter's syndrome, rheumatoid arthritis, scleroderma, Sjogren's syndrome, systemic anaphylaxis, systemic lupus erythematosis, systemic sclerosis, thrombocytopenic purpura, ulcerative colitis, uveitis, Werner syndrome, complications of cancer, hemadialysis, and extracoporeal circulation); viral, fungal, bacterial or

protozoan infections; trauma; and reproductive disorders (e.g. prolactin production disorders, infertility including tubal disease, ovulatory defects, and endometriosis, disruptions of the estrous and menstrual cycles, polycystic ovary syndrome, ovarian hyperstimulation syndrome, endometrial and ovarian tumors, uterine fibroids, autoimmune disorders, ectopic pregnancy, and teratogenesis, breast cancer, fibrocystic breast disease, and galactorrhea, disruptions of spermatogenesis, abnormal sperm physiology, testis cancer, **prostate cancer**, benign prostatic hyperplasia, prostatitis, Peyonie's disease, male breast carcinoma, and gynecomastia). The HPAP-1 **polynucleotide** is a source of probes and primers which bind may be used to detect the **polynucleotide** in a sample from a patient. The HPAP-1 **polynucleotide** may also be administered as part of a gene therapy regime.

ADVANTAGE - None given.

Dwg.0/3

L31 ANSWER 2 OF 48 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 2000-147267 [13] WPIDS
AB WO 200000594 A UPAB: 20000313

NOVELTY - Human transferase (HUTRAN) polypeptide (I), comprising a 454 (Ia), 425 (Ib) or 447 (Ic) amino acid sequence given in the specification, or their fragments, are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a polypeptide variant with at least 90% identity to (I);

(2) a **polynucleotide** (II) encoding (I), comprising the 1975 bp, 2125 bp or 2223 bp sequences given in the specification, with at least 70% identity to, **hybridizes** to, or is complementary to (II);

(3) a vector comprising at least a fragment of (II);

(4) a host cell comprising the vector of (3);

(5) producing (I), comprising culturing the host cell of (4) and recovering (I) from the culture;

(6) a purified antibody which specifically binds (I);

(7) a purified agonist of (I);

(8) a purified antagonist of (I);

(9) treating or preventing an autoimmune/inflammatory disorder or a cancer, comprising administering the antagonist of (8);

(10) treating or preventing a neurological, reproductive or gastrointestinal disorder, comprising administering a pharmaceutical composition comprising (I); and

(11) detecting a **polynucleotide** encoding (I) in a biological sample, comprising **hybridizing** a **polynucleotide** that is complementary to (II) to at least one of the nucleic acids in the sample, and detecting the **hybridization** complex formed (optionally, the nucleic acids in the sample are amplified by **PCR** prior to detection).

ACTIVITY - Contraceptive; cytostatic; antianemic; nootropic; neuroprotective; antiallergic; immunosuppressive; antianemic; antiarrhthymic; antiasthmatic; antiinflammatory; cardiant; hepatotropic; laxative; antidepresant; antidiabetic; antidiarrheic; anticonvulsant; nephrotropic; antigout; antithyroid; thyrominetic; hypotensive; gynecological; antimigraine; antimetic; anorectic; neuroleptic; thrombolytic; tranquilizer; vulnerary; antiulcer; ophthalmological; anti-HIV; cerebroprotective; hemostatic; antibacterial; antiparkinsonian; neuroleptic.

MECHANISM OF ACTION - Gene therapy.

USE - The human transferase (HUTRAN) polypeptides, **polynucleotides**, agonists, antagonists, compositions and

antibodies can be used to diagnose, treat or prevent autoimmune/inflammatory (e.g. AIDS, Addison's disease, adult respiratory distress syndrome, allergies, ankylosing spondylitis, amyloidosis, anemia, asthma, atherosclerosis, autoimmune thyroiditis, bronchitis, cholecystitis, dermatitis, Crohn's disease, dermatomyositis, diabetes mellitus, emphysema, episodic lymphopenia with lymphocytotoxins, erythroblastosis fetalis, erythema nodosum, atrophic gastritis, glomerulonephritis, Goodpasture's syndrome, gout, Grave's disease, Hashimoto's thyroiditis, hypereosinophilia, irritable bowel syndrome, multiple sclerosis, myasthenia gravis, myocardial or pericardial inflammation, osteoarthritis, osteoporosis, pancreatis, polymyositis, psoriasis, Reiter's syndrome, rheumatoid arthritis, scleroderma, Sjogren's syndrome, systemic anaphylaxis, systemic lupus erythematosis, systemic sclerosis, thrombocytopenic purpura, ulcerative colitis, uveitis, Werner syndrome, complications of cancer, hemadialysis, and extracoporeal circulation; viral, fungal, bacterial or protozoan infections; and trauma), neurological disorders (e.g. epilepsy, ischemic cerebrovascular disease, stroke, cerebral neoplasms, Alzheimer's disease, Picks disease, Huntingdon's disease, dementia, Parkinson's disease and other extrapyramidal disorders, amyotropic lateral sclerosis, progressive neural muscular atrophy, retinitis pigmentosa, hereditary ataxias, meningitis, brain abscess, subdural empyema, epidural abscess, suppurative intracranial thrombophlebitis, myelitis, radiculitis, viral central nervous system disease, prion diseases including kuru, Creutzfeldt-Jakob disease and Gerstmann-Straussler-Scheinker syndrome, fatal familial insomnia, neurofibromatosis, tuberous sclerosis, cerebelloretinal hemangioblastomatosis, encephalotrigeminal syndrome, mental retardation, central nervous system developmental disorders, cerebral palsy, neuroskeletal disorders, autonomic nervous system disorders, cranial nerve disorders, spinal cord diseases, muscular dystrophy, neuromuscular disorders, peripheral nervous system disorders, dermatomyositis, polymyositis, myopathies, myasthemia gravis, periodic paralysis, mental disorders, schizophrenic, anxiety, akathemia, amnesia, catatonia, diabetic neuropathy, tardive dyskinesia, dystonias, paranoid psychoses, postherpetic neuralgia and Tourette's disorder), reproductive disorders (e.g. prolactin production disorders, infertility including tubal disease, ovulatory defects, and endometriosis, disruptions of the estrous and menstrual cycles, polycystic ovary syndrome, ovarian hyperstimulation syndrome, endometrial and ovarian tumors, uterine fibroids, autoimmune disorders, ectopic pregnancy, and teratogenesis, breast cancer, fibrocystic breast disease, and galactorrhea; disruptions of spermatogenesis, abnormal sperm physiology, testis cancer, **prostate cancer**, benign prostatic hyperplasia, prostatitis, Peyronie's disease, male breast carcinoma, and gynecomastia) and gastrointestinal disorders (e.g. dysphagia, peptic esophagitis, esophageal spasm and stricture, esophageal carcinoma, dyspepsia, indigestion, gastritis, gastric carcinoma, anorexia, nausea, emesis, gastroparesis, antral or pyloric edema, abdominal angina, pyrosis, gastroenteritis, intestinal obstruction, intestinal tract infections, peptic ulcer, cholelithiasis, cholestasis, cholecystitis, colitis, Whipple's disease, Mallory-Weiss syndrome, irritable bowel syndrome, short bowel syndrome, diarrhea, constipation, gastrointestinal hemorrhage, and AIDS enteropathy) and cancer (e.g. adenocarcinoma, leukemia, melanoma, myeloma, sarcoma, and various cancers). The HUTRAN **polynucleotide**

is a source of probes and primers which bind may be used to detect the **polynucleotide** in a sample from a patient (claimed). The **polynucleotide** may also be administered as part of a gene therapy regime.

ADVANTAGE - None given.

Dwg.0/3

L31 ANSWER 3 OF 48 MEDLINE

2000136052 Document Number: 20136052. Overexpression of kinase-associated phosphatase (KAP) in breast and **prostate cancer** and inhibition of the transformed phenotype by antisense KAP expression. Lee S W; Reimer C L; Fang L; Iruela-Arispe M L; Aaronson S A. (Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Institutes of Medicine, Harvard Medical School, Boston, Massachusetts 02115, USA.. slee2@caregroup.harvard.edu) . MOLECULAR AND CELLULAR BIOLOGY, (2000 Mar) 20 (5) 1723-32. Journal code: NGY. ISSN: 0270-7306. Pub. country: United States. Language: English.

AB Accumulating evidence suggests that phosphatases play an important role in regulating a variety of signal transduction pathways that have a bearing on cancer. The kinase-associated phosphatase (KAP) is a human dual-specificity protein phosphatase that was identified as a Cdc2- or Cdk2-interacting protein by a yeast two-**hybrid** screening, yet the biological significance of these interactions remains elusive. We have identified the KAP gene as an overexpressed gene in breast and **prostate cancer** by using a phosphatase domain-specific differential-display **PCR** strategy. Here we report that breast and prostate malignancies are associated with high levels of KAP expression. The sublocalization of KAP is variable. In normal cells, KAP is primarily found in the perinuclear region, but in tumor cells, a significant portion of KAP is found in the cytoplasm. Blocking KAP expression by antisense KAP in a tetracycline-regulatable system results in a reduced population of S-phase cells and reduced Cdk2 kinase activity. Furthermore, lowering KAP expression led to inhibition of the transformed phenotype, with reduced anchorage-independent growth and tumorigenic potential in athymic nude mice. These findings suggest that therapeutic intervention might be aimed at repression of KAP gene overexpression in human breast and **prostate cancer**.

L31 ANSWER 4 OF 48 MEDLINE DUPLICATE 1

2000129605 Document Number: 20129605. Hematopoietic-specific expression of MEFV, the gene mutated in familial Mediterranean fever, and subcellular localization of its corresponding protein, pyrin. Tidow N; Chen X; Muller C; Kawano S; Gombart A F; Fischel-Ghodsian N; Koeffler H P. (Department of Medicine and Department of Pediatrics and Medical Genetics, Cedars-Sinai Medical Center, UCLA School of Medicine, Los Angeles, CA 90048, USA.) BLOOD, (2000 Feb 15) 95 (4) 1451-5. Journal code: A8G. ISSN: 0006-4971. Pub. country: United States. Language: English.

AB Familial Mediterranean fever (FMF) is a recessively inherited disorder characterized by recurrent, self-limited attacks of fever and serositis and by infiltration of affected tissues by large numbers of neutrophils. A candidate gene for FMF was identified by positional cloning and named "MEFV." The corresponding protein was named "pyrin." To elucidate the currently unknown function of pyrin, we characterized its tissue distribution, regulation of expression during hematopoietic differentiation, and subcellular localization. Reverse transcription-

polymerase chain reaction analysis, followed by **hybridization** with an internal **oligonucleotide**, demonstrated expression of MEFV in different populations of peripheral blood cells. Among hematopoietic cell lines, MEFV was almost exclusively expressed in cells of the myeloid lineage. Furthermore, MEFV messenger RNA was strongly expressed within 24 hours of dimethyl sulfoxide-induced granulocytic differentiation of HL-60 cells. Analysis of complementary DNA from human solid tumor-derived cell lines revealed expression of MEFV in several cell lines derived from colon and **prostate cancers**. Expression of MEFV fused to enhanced green fluorescent protein showed that pyrin localized in distinct patches in the cytoplasm, forming a perinuclear cap. Taken together, MEFV is predominantly expressed in myeloid cells and upregulated during myeloid differentiation, and the corresponding protein, pyrin, is expressed in the cytoplasm. (Blood. 2000;95:1451-1455)

L31 ANSWER 5 OF 48 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 2
1999:811368 Document No. 132:46950 sequence and therapeutic applications for human Nek-related and bub1-related protein kinases. Plowman, Gregory; Martinez, Ricardo; Zhu, Yingfang (Sugen, Inc., USA). PCT Int. Appl. WO 9966051 A2 19991223, 155 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US13533 19990615. PRIORITY: US 1998-89520 19980616; US 1998-98265 19980828.

AB The present invention relates to BUB1 and NEK kinase polypeptides, nucleotide sequences encoding the kinase polypeptides, as well as various products and methods useful for the diagnosis and treatment of various kinase-related diseases and conditions. Through the use of a targeted **PCR** cloning strategy, the human BUB1 serine/threonine kinase was identified and its protein structure was predicted. Addnl., through the use of a bioinformatics strategy, three mammalian members of the NEK-subfamily of STK's have been identified and their protein structure predicted. Assays were structured to monitor a change in cell phenotype or the interaction between the kinases listed here and a natural binding partner. Also methods for treating a disease by administering to a patient the BUB1 kinase are relayed also. These diseases may include leukemia, cervical cancer, lymphoma, colon cancer, lung cancer, melanoma, ovarian cancer, CNS cancer, **prostate cancer**, kidney cancer, or breast cancer. Probes are described which **hybridizes** to target regions of the bub1 gene. Specific immunoreagents to BUB1 kinase were generated. Cell cycle regulation of BUB1 was shown. This protein was localized to microtubules. There is evidence for BUB1 protein autophosphorylation. A high-throughput screening protocol for BUB1 protein kinase inhibitors is given. Baculoviral expression systems are provided. The Makegene Bioinformatics EST assembler was employed.

L31 ANSWER 6 OF 48 CAPLUS COPYRIGHT 2000 ACS
1999:795960 Document No. 132:45834 Polymorphic markers of the gene encoding prostate carcinoma tumor antigen-1 (PCTA-1) and their diagnostic and prognostic applications. Blumenfeld, Marta; Bougueleret, Lydie; Chumakov,

Ilya (Genset, Fr.). PCT Int. Appl. WO 9964590 A1 19991216, 339 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-IB1072 19990604. PRIORITY: US 1998-88187 19980605; US 1998-102324 19980928.

AB The invention concerns the genomic sequence and cDNA sequences of the PCTA-1 gene. The invention also concerns biallelic markers of the PCTA-1 gene and the assocn. established between these markers and **prostate cancer**. The cDNA sequence encoding a mouse homolog of the PCTA-1 protein is also provided. The invention provides means to det. the predisposition of individuals to **prostate cancer** as well as means for the diagnosis of **prostate cancer** and for the prognosis/detection of an eventual treatment response to agents acting against **prostate cancer**.

L31 ANSWER 7 OF 48 CAPLUS COPYRIGHT 2000 ACS

1999:691243 Document No. 131:307694 Biallelic markers for use in constructing a high density disequilibrium map of the human genome. Cohen, Daniel; Blumenfeld, Marta; Chumakov, Ilya (Genset, Fr.). PCT Int. Appl. WO 9954500 A2 19991028, 229 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-IB822 19990421. PRIORITY: US 1998-82614 19980421; US 1998-109732 19981123.

AB The present invention relates to genomic maps comprising biallelic markers, new biallelic markers, and methods of using biallelic markers. Primers **hybridizing** to regions flanking these biallelic markers are also provided. This invention provides **polynucleotides** and methods suitable for genotyping a nucleic acid contg. sample for one or more biallelic markers of the invention. Further, the invention provides a no. of methods utilizing the biallelic markers of the invention including methods to detect a statistical correlation between a biallelic marker allele and a phenotype and/or between a biallelic marker haplotype and a phenotype. The compns. and methods of the invention also find use in the identification of targets for the development of pharmaceutical agents and diagnostic methods, as well as the characterization of differential efficacious responses to and side effects from pharmaceutical agents acting on a disease (e.g., Alzheimer's disease, **prostate cancer**, or asthma) as well as other treatments. The invention claims 3934 biallelic marker sequences, as well as the primer pairs for amplification and detection of each marker; however, the Sequence Listing is not actually provided in the document.

L31 ANSWER 8 OF 48 CAPLUS COPYRIGHT 2000 ACS

1999:194296 Document No. 130:233235 15S-Lipoxygenase protein and cDNA and reagents and methods useful for detecting diseases of the prostate. Billing-Medel, Patricia A.; Cohen, Maurice; Colpitts, Tracey L.; Friedman, Paula N.; Gordon, Julian; Granados, Edward N.; Hodges, Steven C.; Klass,

Michael R.; Kratochvil, Jon D.; Russell, John C.; Stroupe, Stephen D. (Abbott Laboratories, USA). PCT Int. Appl. WO 9913111 A1 19990318, 101 pp. DESIGNATED STATES: W: CA, JP; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US18983 19980911. PRIORITY: US 1997-927978 19970911.

AB Sequences useful for the detecting, diagnosing, staging, monitoring, prognosticating, in vivo imaging, preventing or treating, or detg. the predisposition of an individual to diseases and conditions of the prostate, such as **prostate cancer**, are described. These sequences are derived from prostate tumor tissue and designated as PS213 sequences herein. PS213 is a newly discovered cDNA encoding a human 15S-lipoxygenase comprising 676 amino acids with a calcd. mol. mass of 76 kDa. Also provided are antibodies which specifically bind to PS213-encoded polypeptide or protein, and agonists or inhibitors which prevent action of the tissue-specific PS213 polypeptide, which mols. are useful for the therapeutic treatment of prostate diseases, tumors or metastases.

L31 ANSWER 9 OF 48 CAPLUS COPYRIGHT 2000 ACS

1999:704894 Document No. 131:307661 A sensitive RT-**PCR** method for molecular staging of **prostate cancer** using PSA antigen mRNA. Katz, Aaron E.; Buttyan, Ralph; Raffo, Anthony; Olsson, Carl A. (The Trustees of Columbia University in the City of New York, USA). U.S. US 5976794 A 19991102, 31 pp., Cont.-in-part of U.S. Ser. No. 229,391, abandoned. (English). CODEN: USXXAM. APPLICATION: US 1997-718547 19970113. PRIORITY: US 1994-229391 19940415; WO 1995-US4680 19950414.

AB The development of an extremely sensitive "enhanced" **PCR**-based assay that allows to identify prostate-specific antigen (PSA)-synthesizing cells even when they are highly dild. in a population of peripheral lymphocytes is described. The method comprises (a) extg. mRNA from a biol. sample: (b) contacting the mRNA with reverse transcriptase under conditions allowing for the prodn. of cDNA; (c) contacting the cDNA with a pair of reverse transcriptase **PCR** primers capable of specifically **hybridizing** with DNA encoding PSA wherein one such primer is an **oligonucleotide** of 12 to 30 nucleotides in length and comprises the sequence 5-CACCCATCCTA-3' and wherein the second such primer is an **oligonucleotide** of 12 to 30 nucleotides in length and comprises the sequence 5'-TCCAGCCACGAC-3'; and wherein at least one of the primers is covalently linked to a modified digoxigenin mol. and under conditions allowing for extension of the primers; and (d) detecting the resulting amplified DNA.

L31 ANSWER 10 OF 48 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD

AN 2000-116557 [10] WPIDS

AB WO 9964631 A UPAB: 20000228

NOVELTY - Nucleic acid markers of prostate, breast and bladder cancer are new. The markers are indicators of malignant transformation of prostate, breast and bladder tissues and are diagnostic of the potential for metastatic spread of malignant prostate tumors.

DETAILED DESCRIPTION - An isolated nucleic acid segment comprising a full length sequence or the full length complement of a sequence selected from the sequences (A)-(T) of 391, 614, 757, 673, 358, 166, 107, 183, 92, 174, 132, 135, 471, 209, 407, 267, 333, 369, 301 and 25 bp, respectively (T) or 135 amino acid (aa) sequence (U) (sic) (all sequences are given in the specification).

INDEPENDENT CLAIMS are also included for the following:

(1) an isolated nucleic acid molecule (NAM), of 14-100 bp, identical in sequence to a contiguous portion of at least 14 bp of (A)-(U);

(2) an isolated polypeptide with an aa sequence encoded by (A)-(S);

(3) an isolated peptide of 10-050 aa with an aa sequence encoded by (A)-(S);

(4) identifying markers for human **prostate cancer** by:

(a) providing human prostate RNAs;

(b) amplifying the RNAs;

(c) separating the amplification products;

(d) identifying RNAs that are differentially expressed between human **prostate cancers** versus normal/benign human prostate;

(5) detecting **prostate cancer** cells in biological sample by detecting a **prostate cancer** marker which is a **polynucleotide** selected from (A)-(U), and the 610 bp (V), 1649 bp (W) or 175 bp (X) sequences given in the specification;

(6) treating **prostate cancer** by:

(a) obtaining a **prostate cancer** tissue sample;

(b) screening the sample for expression of a polypeptide encoded by (A)-(U);

(c) providing an antibody that reacts immunologically against the polypeptide, and

(d) administering the antibody;

(7) treating **prostate cancer** by:

(a) as in (6a) and (6b);

(b) providing an antisense DNA molecule encoding a RNA molecule that binds to the **polynucleotide**;

(c) providing the antisense DNA molecule in the form of a human vector containing regulatory elements for the production of the RNA molecule; and

(d) administering the vector;

(8) a kit for detecting **prostate cancer** cells in a biological sample, comprising a primer pair for amplifying (A)-(U), and containers for each of the primers;

(9) a kit for detecting **prostate cancer** cells comprising a primer pair for amplifying a nucleic acid product of a human gene selected from cyclin A, fibronectin, and a truncated form of Her2/neu, and containers for each of the primers;

(10) a kit for detecting **prostate cancer** cells comprising an **oligonucleotide** probe (ON) which binds to a sequence (A)-(U), and a container for the probe;

(11) a kit for detecting **prostate cancer** cells comprising ON probe binding to a nucleic acid product of a human gene as in (9), and a container for the probe;

(12) a kit for detecting **prostate cancer** cells comprising an antibody which binds to a protein encoded by (A)-(U), and a container for the antibody;

(13) detecting **prostate cancer** cells comprising:

(a) providing an antibody binding as in (12) and to a truncated form of Her2/neu;

(b) contacting a human tissue sample with the antibody;

(c) separating bound from unbound antibody; and

(d) detecting the bound antibody;

(14) a kit for detecting prostate cancer cells comprising an antibody binding as in (13), and container for the antibody;

(15) treating prostate cancer by:

(a) selecting a prostate cancer marker selected from (A)- (U), cyclin A, fibronectin and a truncated form of Her2/neu;

(b) providing an inhibitor designed to bind specifically to the

protein product of the marker; and

(c) administering the inhibitor;

(16) an isolated nucleic acid segment used as a marker of bladder cancer or breast cancer, and having a sequence or the complement of a sequence selected from (C), (T) or (U);

(17) an isolated NAM, of 14-100 bases, identical in sequence to a contiguous portion of at least 14 bases of (C), (T) or (U);

(18) an isolated polypeptide encoded by (C), (T) or (U);

(19) an isolated peptide of 10-50 aa, encoded by (C), (T) or (U);

(20) detecting bladder cancer or breast cancer cells by detecting a bladder or breast cancer marker having the sequence (C), (T) or (U);

(21) treating bladder or breast cancer by:

(a) obtaining a cancer tissue sample;

(b) screening the sample for the expression of a polypeptide encoded by (C), (T) or (U);

(c) providing an antibody against the polypeptide, and

(d) administering the antibody;

(22) treating bladder or breast cancer by:

(a) as in (21a) and (21b);

(b) providing an antisense DNA molecule that encodes a RNA molecule that binds to the polynucleotide;

(c) providing the antisense DNA molecule in the form of a human vector containing regulatory elements for the production of the RNA molecule; and

(d) administering the vector;

(23) a kit for detecting bladder cancer or breast cancer cell, comprising a primer pair for amplifying (C), (T) or (U), ON probe which binds to (C), (T) or (U), or an antibody which binds to the protein encoded by (C), (T) or (U), and

(24) detecting bladder or breast cancer cells by:

(a) providing an antibody that binds to a polypeptide encoded by (C), (T) or (U);

(b) contacting a human tissue sample with the antibody;

(c) separating bound from unbound antibody; and

(d) detecting the bound antibody.

USE - The nucleic acid markers of the invention can be used as markers of prostate cancer, benign prostatic hyperplasia (BPH), bladder cancer or breast cancer, and as targets for therapeutic intervention in prostate cancer, BPH, bladder cancer or breast cancer. The markers may also be used to design specific probes and primers, for the rapid analysis of prostate, bladder or breast biopsy samples. The probes and primers may also be used for in situ hybridization or in situ PCR detection and diagnosis. They may also be used to identify and isolate full length gene sequences form various DNA libraries. Antibodies against the polypeptide products of the markers can be used to treat prostate cancer, bladder cancer or breast cancer. The encoded proteins may be used to detect antibodies. The proteins and antibodies can be used in immunodetection methods for detecting or quantifying the cancers, and for clinical diagnosis of these cancers. The antibodies may also be used for radioimaging to quantify and localize the encoded proteins.

ADVANTAGE - A need exists for the identification of genes which are differentially expressed in prostate, bladder or breast cancer. The present invention meets this need, and provides nucleic acid sequences which can be used in the development of a rapid, inexpensive method to diagnose cancer.

Dwg.0/20

L31 ANSWER 11 OF 48 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 2000-116541 [10] WPIDS

AB WO 9964594 A UPAB: 20000228
NOVELTY - New isolated **prostate cancer** specific nucleic acids are disclosed.

DETAILED DESCRIPTION - A novel method of diagnosing cancer, tumor progression, hyperproliferative cell growth, or accompanying biological and physical manifestations comprises:

(1) providing a **polynucleotide** probe (PN) that comprises a sequence capable of **hybridizing** to any one of the 339 sequences (given in the specification) or complements;

(2) contacting a biological sample for diagnosis with the probe under **hybridizing** conditions that permit formation of a duplex; and

(3) determining the presence of the duplex.

INDEPENDENT CLAIMS are also included for the following:

(1) diagnosing cancer, tumor progression, or hyperproliferative cell growth comprising:

(a) providing an antibody capable of binding to a polypeptide encoded by any one of the 339 sequences or complements;

(b) contacting a biological sample for diagnosis with the antibody to permit formation of an antibody-polypeptide complex; and

(c) determining the presence of the complex;

(2) a diagnostic kit comprising:

(1) a diagnostic reagent comprising a PN probe that comprises a sequence capable of **hybridizing** to any one of the 339 sequences or complements, when the sequence is present in a test biological sample;

(2) a normal biological sample; and

(3) instructions for detecting differences that exist between the levels of duplexes in the test biological sample as compared to the normal biological sample;

(3) a method of treating a mammal with cancer, tumor progression, hyperproliferative cell growth or accompanying biological and physical manifestations, comprising administering to the mammal a composition that comprises a PN comprising a sequence capable of **hybridizing** under stringent conditions to any one of the 339 sequences or complement;

(4) an isolated PN selected from:

(a) a PN comprising a nucleotide sequence (NS) of any one of the 52 sequences (given in the specification);

(b) a PN encoding a variant of a polypeptide encoded by (a); and

(c) a PN encoding a protein expressed by a PN having a sequence of at least one of the sequences as in (a);

(5) a vector comprising a PN as in (4);

(6) a host cell comprising a vector as in (5), and

(7) a composition comprising a polypeptide selected from:

(a) a polypeptide encoded by any one of the PNs as in (4); and

(b) a variant of a polypeptide as in (a).

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - None given.

USE - The products and methods can be used for the diagnosis, prognosis, and treatment of cancer, tumor progression, hyperproliferative cell growth, and accompanying physical and biological manifestations. They can be used particularly for prostatic disorders such as metastatic **prostate cancer**, localized **prostate cancer**, or benign prostate hyperplasia (BPH).

Dwg.0/3

L31 ANSWER 12 OF 48 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 2000-072832 [06] WPIDS
AB WO 9962941 A UPAB: 20000203
NOVELTY - Isolated STRAP-1 protein (I) having a 376 amino acid (aa) sequence (1), fully defined in the specification, and isolated STRAP-2 protein (II) having a partial 173 aa sequence (2), fully defined in the specification.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) polypeptide (III) containing at least 15 contiguous aa from (1) or (2);

(2) polypeptide (Ia) at least 90% identical with (1) over its entire length;

(3) an isolated **polynucleotide** (IV) which:

(a) is a 1195 bp or 520 bp sequence, fully defined in the specification, or their RNA equivalents;

(b) encodes STRAP-1 as encoded by the cDNA in plasmid 8P104 clone 10.1 (ATCC 98849); or

(c) encodes STRAP-1 or -2;

(4) **polynucleotides** fully complementary to (IV);

(5) recombinant expression vector containing (IV) that encodes STRAP-1;

(6) host cells containing this vector;

(7) recombinant production of STRAP-1 by culturing cells of (6);

(8) STRAP-1 produced this way;

(9) antibodies (Ab) that stain 293T cells transformed with a STRAP-1-expressing plasmid, but not untransformed cells, or bind specifically to STRAP-1 or -2, or their fragments (III);

(10) fragments of Ab;

(11) recombinant protein (V) containing the antigen-binding domain of Ab;

(12) detecting STRAP-1 or -2 from their reaction with Ab, or its fragments or (V);

(13) detecting STRAP-1 or -2 **polynucleotide** by **hybridization** with specific probes;

(14) detecting STRAP-1 or -2 mRNA by reverse transcription and amplification;

(15) composition for treating **prostate cancer** containing Ab that bind to the extracellular domain of STRAP-1 or -2; and

(16) composition for treating colon or bladder cancer containing Ab that binds to the extracellular domain of STRAP-1.

ACTIVITY - Anticancer.

MECHANISM OF ACTION - STRAP proteins may be ion-channel or gap-junction proteins. Immunization with STRAP induces cellular and humoral immune responses against STRAP-expressing cells.

USE - (I) and (II) are cell-surface tumor antigens. They are used:

(1) to generate specific antibodies (Ab);

(2) to identify specific-binding agents and

(3) to produce anticancer vaccines.

Ab are used:

(1) as immunoassay reagents for detection, prognosis, and monitoring of cancers (or susceptibility);

(2) as therapeutic inhibitors (including where conjugated to a toxin or therapeutic agent), for treating particularly cancer of prostate, colon and bladder;

(3) for affinity purification of STRAP proteins;

(4) for isolating STRAP homologs or related molecules and

(5) for raising anti-idiotypic antibodies that mimic STRAP, useful in

vaccines.

Nucleic acids (IV) that encode STRAP are used:

(1) for recombinant protein production;

(2) as source of primers and probes for diagnostic and prognostic detection of STRAP nucleic acid, for identifying STRAP-expressing cells and for screening inhibitors of STRAP expression and

(3) for therapeutic modulation/inhibition of STRAP expression.

ADVANTAGE - Since STRAP proteins are exposed on the surface at high level, they are easily targeted by systemically administered agents, and because they are expressed mainly on prostatic epithelial cells, agents targeted to them should have minimal side effects on other tissues.

Dwg.0/20

L31 ANSWER 13 OF 48 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD

AN 2000-062303 [05] WPIDS

AB WO 9958692 A UPAB: 20000128

NOVELTY - A substantially purified Human Apoptosis associated protein (HAPOP)(I) comprising an amino acid (a.a) sequence selected from HAPOP-1,

HAPOP-2, HAPOP-3, HAPOP-4 and their fragments is new.

DETAILED DESCRIPTION - (I) is selected from fully defined (a.a) sequences of HAPOP 1,2,3,4 and their fragments containing 480,238,410 and

211 (a.as) respectively. INDEPENDENT CLAIMS are also included for the following: (i) an isolated and purified **polynucleotide** encoding HAPOP (II); (ii) an isolated and purified **polynucleotide** complementary to (II); (iii) an expression vector comprising at least a fragment of (II); (iv) a host cell comprising the expression vector; (v) producing (I) comprising of host cell culture under conditions suitable for expressing and recovering (I); (vi) a purified antibody which specifically binds to (I); (vii) a purified agonist of (I); (viii) a purified antagonist of (I); (ix) detecting (II) comprising **hybridizing** a complementary **polynucleotide** to at least one of the nucleic acids in the biological sample and detecting the **hybridization** complex, presence of which correlates with the presence of (II).

ACTIVITY - Antiarteriosclerotic; cytostatic; anti arthritic; hepatotropic (no supporting data given).

MECHANISM OF ACTION - Apoptosis regulator.

USE - A pharmaceutical composition comprising (I) in conjunction with a carrier (claimed), a purified antagonist of (I) (claimed), vectors

and agonists of (I) are administered for diagnosing, treating or preventing disorders associated with increased or decreased apoptosis (claimed), e.g. cell proliferative disorders such as atherosclerosis, arteriosclerosis and cancers; immune disorders such as rheumatoid arthritis, systemic lupus erythematosus; reproductive disorders such as **prostate cancer**, endometrial and ovarian tumors; and gastrointestinal disorders such as cirrhosis, colitis, hepatitis and pancreatitis. The **polynucleotides** may be useful to detect and quantitate expression of (I) gene which is correlated with disease and is also useful to detect differences in the chromosomal location due

to translocation, inversion etc., among normal, carrier, or affected individuals.

ADVANTAGE - The combination of the therapeutic agents may act synergistically to effect the treatment or prevention of various disorders providing improved efficacy with lower dosages of each agent and thus reducing the potential for adverse side effects.

Dwg.0/3

L31 ANSWER 14 OF 48 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 2000-039068 [03] WPIDS
AB WO 9958560 A UPAB: 20000118
NOVELTY - (A) A novel isolated Prostapin (PS) protein has an amino acid (aa) sequence (S1) of 379 aa or a polypeptide fragment.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) an isolated PS polypeptide comprising an aa sequence which is at least 70% identical to (S1) over its entire length;
(2) an isolated **polynucleotide** (PN) encoding a PS protein as in (A);
(3) an isolated PN encoding a PS polypeptide whose sequence is encoded by a cDNA contained in plasmid pProstapin deposited as ATCC No. 98757;
(4) an isolated PN selected from:
(a) a PN having a sequence (S2) of 1882 nucleotides (nt), where T can also be U;
(b) a PN fully complementary to (a); and
(c) a PN which **hybridizes** under stringent conditions to (a) or (b);
(5) a recombinant expression vector which contains a PN as in (4);
(6) a host cell which contains an expression vector as in (5);
(7) an antibody which binds to a PS protein as in (A);
(8) a recombinant protein comprising an antigen binding domain of an antibody as in (7);
(9) an assay for identifying a cell which expresses a PS gene comprising detecting the presence of PS mRNA in a cell;
(10) an assay for identifying a cell which expresses a PS gene comprising detecting the presence of PS protein in a cell, and
(11) a recombinant viral vector which contains a PN encoding a PS protein as in (A).
USE - The PS may function as a prostate-specific tumor suppressor, apoptosis-inducer or apoptosis-modulator. The PS gene and protein, as well as factors capable of activating PS expression, may be useful as therapeutic agents capable of restoring critical tumor suppressor activity lost in advanced **prostate cancer**. In addition PS may represent an ideal marker for predicting and identifying progression to advanced stage and metastatic **prostate cancer**, and may also be useful for determining susceptibility to advanced disease and for gauging prostate tumor aggressiveness. Therapeutic strategies which restore PS to prostate tumor cells may result in inhibition of primary prostate tumors and **prostate cancer** metastasis, tumor regression, and/or an inhibition in the rate or extent of disease progression.
Dwg.0/13

L31 ANSWER 15 OF 48 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 2000-062165 [05] WPIDS
CR 2000-038791 [01]
AB WO 9957565 A UPAB: 20000330
NOVELTY - Methods for detecting and evaluating cancer that are based on the finding that OB-cadherin and N-cadherin are expressed by metastatic carcinoma cells, but not by highly differentiated, poorly invasive carcinomas, are new.
DETAILED DESCRIPTION - A novel method for determining the presence or absence of a cancer in a patient comprises:
(1) contacting a biological sample from the patient with a binding

agent that specifically binds to OB- or N-cadherin OR with an **oligonucleotide** that **hybridizes** to a **polynucleotide** that encodes OB- or N-cadherin, and

(2) detecting in the sample an amount of polypeptide that binds to the binding agent OR the amount of **polynucleotide** that **hybridizes** to the **oligonucleotide**, relative to a predetermined cut-off value, and determining the presence or absence of cancer in the patient from this.

INDEPENDENT CLAIMS are also included for the following:

(1) monitoring the progression of cancer in a patient by:

(a) contacting a biological sample obtained from a cancer patient at a first point in time with a binding agent that specifically binds to OB- or N-cadherin OR with an **oligonucleotide** that **hybridizes** to a **polynucleotide** that encodes OB- or N-cadherin;

(b) detecting in the sample an amount of polypeptide that binds to the binding agent OR the amount of **polynucleotide** that **hybridizes** to the **oligonucleotide**;

(c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and

(d) comparing the amount of polypeptide OR **polynucleotide** detected in (c) with that detected in (b), and so monitoring the progression of cancer in the patient;

(2) evaluating the metastatic potential of a cancer in a patient by:

(a) contacting a biological sample obtained from a cancer patient with a binding agent as in (1a), and

(b) detecting the polypeptide in the sample that binds to the binding agent OR the amount of **polynucleotide** that **hybridizes** to the **oligonucleotide**, relative to a predetermined cut-off value, and from here evaluating the metastatic potential of the cancer in the patient;

(3) a diagnostic kit comprising one or more monoclonal antibodies that specifically bind to an OB-cadherin cellular adhesion recognition (CAR) sequence and a detection reagent, and

(4) a diagnostic kit comprising an **oligonucleotide** that **hybridizes** to a **polynucleotide** encoding OB-cadherin, or to the complement of such a **polynucleotide**; and a second **oligonucleotide** 10-40 nucleotides in length.

USE - The methods can be used to determine the metastatic potential of a cancer. The methods may be used to detect a metastatic cancer in a patient, to monitor progression of a cancer, or to evaluate the metastatic potential of a cancer (all claimed). Cancers which may be evaluated using the methods include leukemia, **prostate cancer**, breast cancer and ovarian cancer (claimed).

ADVANTAGE - At present, there is no accurate method for evaluating the metastatic potential of prostate and other cancers. In order to improve cancer treatment and survival, techniques that permit a more accurate diagnosis are needed. The invention provides a method that accurately evaluates the metastatic potential of a cancer, which is useful for early diagnosis and treatment.

Dwg.0/8

L31 ANSWER 16 OF 48 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD

AN 2000-052971 [04] WPIDS

AB WO 9957270 A UPAB: 20000124

NOVELTY - A substantially purified human receptor molecule, REC polypeptide (I), comprising one of the 26 amino acid sequences given in the specification, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a polypeptide variant with at least 90 % identity to (I);

(2) a **polynucleotide** (II) encoding (I), comprising the one of the 16 **polynucleotide** sequences given in the specification;

(3) a **polynucleotide** with at least 90 % identity to (II);

(4) a **polynucleotide** which **hybridizes** under stringent conditions to (II);

(5) a **polynucleotide** which is complementary to (II);

(6) an expression vector comprising at least a fragment of (II);

(7) a host cell comprising the expression vector of (6);

(8) a method for producing (I), comprising culturing the host cell of (7) and recovering (I) from the culture;

(9) a pharmaceutical composition comprising (I);

(10) a purified antibody which specifically binds (I);

(11) a purified agonist or antagonist of (I);

(12) a method for treating or preventing a neoplastic, immunological, reproductive gastrointestinal, nervous, smooth muscle or musculoskeletal disorder, comprising administering to a subject an effective amount of the antagonist of (11);

(13) a method for detecting a **polynucleotide** encoding (I) in a biological sample containing nucleic acids, comprising **hybridizing** the **polynucleotide** of (5) to at least one of the nucleic acids in the sample, and detecting the **hybridization** complex formed (optionally, the nucleic acids in the sample are amplified by **PCR** prior to detection).

ACTIVITY - Antiinfertility; cytostatic; antianemic; nootropic; neuroprotective; antiallergic; immunosuppressive; antiarrhthymic; antiasthmatic; antiinflammatory; cardiant; hepatotropic; laxative; antidepresant; antidiabetic; antidiarrheic; anticonvulsant; nephrotropic; antigout; antithyroid; thyromimetic; hypotensive; gynecological; antimigraine; antimetic; anorectic; neuroleptic; thrombolytic; tranquilizer; vulnerary; antiulcer; ophthalmological; antipsoriatic; immunostimulant; osteopathic; antiarthritic; antirheumatic; antiallergic; antibacterial; fungicide; protozoacide; virucide;

MECHANISM OF ACTION - None given.

USE - Human receptor molecules (RECs) appear to play a role in neoplastic, immunological, reproductive gastrointestinal, nervous, smooth muscle and musculoskeletal disorders. The protein, antagonists and agonists, and compositions can be used to treat a reproductive disorder, including but not limited to, prolactin production disorders; infertility including tubal disease, ovulatory defects, and endometriosis; disruptions of the estrous and menstrual cycles, polycystic ovary syndrome, ovarian hyperstimulation syndrome, endometrial and ovarian tumors, uterine fibroids, autoimmune disorders, ectopic pregnancy, and teratogenesis; breast cancer, fibrocystic breast disease, and galactorrhea; disruptions of spermatogenesis, abnormal sperm physiology, testis cancer, **prostate cancer**, benign prostatic hyperplasia, prostatitis, Peyonie's disease, male breast carcinoma, and gynecomastia. Gastrointestinal disorders include but are not limited to dysphagia, peptic esophagitis, esophageal spasm and stricture, esophageal carcinoma, dyspepsia, indigestion, gastritis, gastric carcinoma, anorexia, nausea, emesis, gastroparesis, intestinal tract infections, peptic ulcer, colitis, Whipple's disease, Mallory-Weiss syndrome, irritable bowel syndrome, short bowel syndrome, diarrhea, constipation, cirrhosis, jaundice, and hepatic

vein thombosis. Nervous disorders include, but are not limited to, Alzheimer's disease, amnesia, bipolar disorder, catatonia, cerebral neoplasms, Down's syndrome, and dystonias. Smooth muscle cell disorders include, but are not limited to angina, anaphylactic shock, arrhymias, cardiovascular shock, migraine, and pheochromocytoma. Musculoskeletal disorders include muscular dystrophy, central core disease, nemaline myopathy, centronuclear myopathy, lipid myopathy, inclusion body myositis, thyrotoxic myoapathy, and ethanol myopathy. Immunological disorders treated include AIDS, Addison's disease, adult respiratory distress syndrome, allergies, ankylosing spondylitis, amyloidosis, anemia, asthma, atherosclerosis, autoimmune hemolytic anemia, autoimmune thyroiditis, bronchitis, cholecystitis, contact dermatitis, Crohn's disease, atopic dermatitis, dermatomyositis, diabetes mellitus, emphysema, episodic lymphopenia with lymphocytotoxins, erythroblastosis fetalis, erythema nodosum, atrophic gastritis, glomerulonephritis, Goodpasture's syndrome, gout, Grave's disease, Hashimoto's thyroiditis, hypereosinophilia, irritable bowel syndrome, multiple sclerosis, myasthenia gravis, myocardial or pericardial inflammation, osteoarthritis, osteoporosis, pancreatitis, polymyositis, psoriasis, Reiter's syndrome, rheumatoid arthritis, scleroderma, Sjogren's syndrome, systemic anaphylaxis, systemic lupus erythematosis, systemic sclerosis, thrombocytopenic purpura, ulcerative colitis, uveitis, Werner syndrome, complications of cancer, hemadialysis, and extracoporeal circulation; viral, fungal, bacterial or protozoan infections; and trauma. Neoplastic disorders include adenocarcinoma, leukemia, melanoma, myeloma, sarcoma, and various cancers.

The REC **polynucleotide** is a source of probes and primers which bind may be used to detect (II) in a sample from a patient (claimed). (II) may also be administered as part of a gene therapy regime.

ADVANTAGE - None given.

Dwg.0/0

L31 ANSWER 17 OF 48 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD

AN 2000-052939 [04] WPIDS

AB WO 9957140 A UPAB: 20000124

NOVELTY - A novel human growth-associated protease inhibitor heavy chain precursor (GAPIP) polypeptide (I), which comprises the 942 amino acid sequence fully defined in the specification, or a fragment of it, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a polypeptide variant with at least 90 % identity to (I);

(2) a **polynucleotide** (II) encoding (I), comprising the 3636 bp sequence fully defined in the specification;

(3) a **polynucleotide** with at least 90 % identity to (II);

(4) a **polynucleotide** which **hybridizes** under stringent conditions to (II);

(5) a **polynucleotide** which is complementary to (II);

(6) an expression vector comprising at least a fragment of (II);

(7) a host cell comprising the expression vector of (6);

(8) a method for producing (I), comprising culturing the host cell of (7) and recovering (I) from the culture;

(9) a pharmaceutical composition comprising (I);

(10) a purified antibody which specifically binds (I);

(11) a purified agonist or antagonist of (I);

(12) a method for treating or preventing a reproductive disorder or a developmental disorder, comprising administering to a subject in need an

effective amount of the composition of (9);

(13) a method for treating or preventing a neoplastic disorder or an immunological disorder, comprising administering to a subject in need an effective amount of the antagonist of (11); and

(14) a method for detecting a **polynucleotide** encoding (I) in a biological sample containing nucleic acids, comprising **hybridizing** the **polynucleotide** of (5) to at least one of the nucleic acids in the sample, and detecting the **hybridization** complex formed (optionally, the nucleic acids in the sample are amplified by **PCR** prior to detection).

ACTIVITY - Immunosuppressive; antiasthmatic; antianemic; antiarteriosclerotic; antithyroid; cardiant; cytostatic; antidiabetic; antigout; thyromimetic; hemostatic; virucide; hepatotropic; anti-HIV; osteopathic; antiparasitic; antipsoriatic; antirheumatic; hepatotrophic; anticonvulsant; antiinfertility; nephrotropic; immunostimulant; antiallergic; antiinflammatory; antithyroid; neuroprotective; osteopathic; antiarthritic; antiulcer; ophthalmological; virucide; antibacterial; antifungal; protozoacide; tranquilizer; vulnery.

MECHANISM OF ACTION - Protease inhibitor.

USE - Human growth-associated protease inhibitor heavy chain precursor (GAPIP) is expressed in cancer, immune, reproductive, gastrointestinal, nervous and fetal tissue, and so appears to play a role in reproductive, developmental, neoplastic and immunological; disorders. The protein, antagonists and agonists, and compositions can be used to treat a reproductive disorder, including but not limited to, prolactin production disorders; infertility including tibal disease, ovulatory defects, and endometriosis; disruptions of the estrous and menstrual cycles, polycystic ovary syndrome, ovarian hyperstimulation syndrome, endometrial and ovarian tumors, uterine fibroids, autoimmune disorders, ectopic pregnancy, and teratogenesis; breast cancer, fibrocystic breast disease, and galactorrhea; disruptions of spermatogenesis, abnormal sperm physiology, testis cancer, **prostate cancer**, benign prostatic hyperplasia, prostatitis, Peyonie's disease, male breast carcinoma, and gynecomastia. Developmental disorders treated include but are not limited to Cushing's syndrome, renal tubular acidosis, anemia, achondroplstic dwarfism, Duchenne and Becker muscular dystrophy, epilepsy, gonadol dysgenesis, WAGR syndrome, Smith-Magenis syndrome, myelodysplastic syndrome, hereditary mucoepithelial dysplasia, hereditary keratomas and neuropathies, hydrocephalus, seizure disorders, and cerebral palsy, spina bifida, congenital glaucoma, cataract, and sensorineural hearing loss. Immunological disorders treated include AIDS, Addison's disease, adult respiratory distress syndrome, allergies, ankylosing spondylitis, amyloidosis, anemia, asthma, atherosclerosis, autoimmune hemolytic anemia, autoimmune thyroiditis, bronchitis, cholecystitis, contact dermatitis, Crohn's disease, atopic dermatitis, dermatomyositis, diabetes mellitus, emphysema, episodic lymphopenia with lymphocytotoxins, erythroblastosis fetalis, erythema nodosum, atrophic gastritis, glomerulonephritis, Goodpasture's syndrome, gout, Grave's disease, Hashimoto's thyroiditis, hypereosinophilia, irritable bowel syndrome, multiple sclerosis, myasthenia gravis, myocardial or pericardial inflammation, osteoarthritis, osteoporosis, pancreatitis, polymyositis, psoriasis, Reiter's syndrome, rheumatoid arthritis, scleroderma, Sjogren's syndrome, systemic anaphylaxis, systemic lupus erythematosis, systemic sclerosis, thrombocytopenic purpura, ulcerative colitis, uveitis, Werner syndrome, complications of cancer, hemadialysis, and extracoporeal circulation; viral, fungal, bacterial or protozoan infections; trauma; and

arteriosclerosis, bursitis, cirrhosis, hepatitis, mixed connective tissue disease, myelofibrosis, paroxysmal nocturnal hemoglobinuria, polycythemia vera, and primary thromobocynemia. Neoplastic disorder include adenocarcinoma, leukemia, melanoma, myeloma, sarcoma, and various cancers.

The GAPIP **polynucleotide** is a source of probes and primers which bind may be used to detect (II) in a sample from a patient (claimed). (II) may also be administered as part of a gene therapy regime.

ADVANTAGE - None given.

Dwg.0/3

L31 ANSWER 18 OF 48 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 2000-062041 [05] WPIDS
AB WO 9955905 A UPAB: 20000128

NOVELTY - Diagnostic or prognostic assay of disorders characterized by abnormal methylation of one or more cytosine (C) residues in the glutathione-S-transferase (GST) Pi gene and/or its regulatory flanking regions, is new.

DETAILED DESCRIPTION - The assay includes:

(i) amplification of a target region in the Pi gene and/or regulatory sequences under conditions which result in amplification only if at least one C is methylated, then detection of the amplicon; or

(ii) detecting abnormal methylation of C defined by the CpG sites -43 to +55, inclusive.

An INDEPENDENT CLAIM is also included for 22 specific probes and primers for use in the assay:

CGCGAGGTTTTCGTTGGAGTTTCGTCGTC;
CGTTATTAGTGAGTACGCGCGGTTC;
YGGTTTTAGGGAATTTTTTTTCGC;
YGGYGYGTTAGTTYGTTGYGTATATTTC;
GGGAATTTTTTTTCGCGATGTTTYGGCGC;
TTTTTAGGGGGTTYGGAGCGTTTC;
GGTAGGTTGYGTTTATCGC;
AAAAATTCRAATCTCTCCGAATAAACG;
AAAAACCRAAATAAAAACCACACGACG;
TCCCATCCCTCCCCGAAACGCTCCG;
GAAACGCTCCGAACCCCCTAAAAACCGCTAACG;
CRCCCTAAAATCCCCRAAATCRCCGCG;
ACCCCRACRACCRCTACACCCCRAACGTCG;
CTCTTCTAAAAAATCCCRCRAACTCCCGCCG;
AAAACRCCCTAAAATCCCCGAAATCGCCG;
AACTCCCRCCGACCCCAACCCCGACGACCG;
AAACCTAAAAAATAAACAAACAA;
GGGCCTAGGGAGTAAACAGACAG;
CCTTTCCCTCTTTCCCARRTCCCCA;
TTTGGTATTTTTTTTCGGGTTTTAG;
CTTGGCATCCTCCCCCGGGCTCCAG; and
GGYAGGGAAGGGAGGYAGGGGYTGGG;
Y = mixture of C and T;
R = mixture of A and G.

USE - The method is used for diagnosis of cancer, particularly of breast, cervix, liver or especially prostate.

Dwg.0/10

L31 ANSWER 19 OF 48 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1999-277272 [23] WPIDS
AB WO 9918210 A UPAB: 19990616

NOVELTY - Isolated polypeptides and DNA obtained from prostate tumor cells

are new.

DETAILED DESCRIPTION - New polypeptides (P) comprise an immunogenic portion of a prostate protein having a partial sequence selected from sequences S1, S2, S3, S4, S5 and S6 having 89, 127, 43, 751, 6 and 16 amino acids in length, respectively, or a variant of the protein that differs only in conservative substitutions and/or modifications.

INDEPENDENT CLAIMS are also included for the following:

(1) a polypeptide comprising an immunogenic portion of a prostate protein or a variant of the protein that differs only in conservative substitutions and/or modifications where the protein comprises an amino acid sequence encoded by a DNA sequence selected from sequences N1, N2-N7, N8, N9 and N10-N13, (which are 2276, 1797, 720, 1996, 3642, 1397, 800, 1810, 1497, 1050, 702, 688, 814 and 966 nucleotides in length, respectively), the complements of these sequences, and DNA sequences that **hybridize** to these sequences or a complement, under moderately stringent conditions;

(2) a DNA molecule comprising a nucleotide sequence (NS) encoding a polypeptide as in (P) or (1);

(3) an expression vector comprising a DNA molecule as in (2);

(4) a host cell transformed with an expression vector as in (3);

(5) a monoclonal antibody that binds to a polypeptide as in (A) or (1);

(6) a vaccine comprising the polypeptide as in (P) or (1) and a non-specific immune response enhancer;

(7) a vaccine comprising a DNA molecule encoding (P) or the proteins as in (1) and a non-specific immune response enhancer;

(8) a pharmaceutical composition for the treatment of **prostate cancer** comprising a polypeptide and a carrier, the polypeptide comprising an immunogenic portion of a prostate protein having a partial sequence selected from sequences S7, S8, S9, S10, S11-S17 and S18-S31 defined in the specification;

(9) a vaccine for the treatment of **prostate cancer** comprising a polypeptide and a non-specific immune response enhancer, the polypeptide comprising an immunogenic portions of a prostate protein having a partial sequence selected from sequences S7, S8, S9, S10, S11-S17 and S18-S31 defined in the specification;

(10) a method for detecting **prostate cancer** in a patient comprising:

(a) contacting a biological sample obtained from a patient with a binding agent which is capable of binding to a polypeptide, the polypeptide comprising either a polypeptide as in (P) or (1), or an immunogenic portion of a prostate protein having a partial sequence selected from sequences S7, S8, S9, S10, S11-S17 and S18-S31 defined in the specification; and

(b) detecting in the sample a protein or polypeptide that binding to the binding agent, thereby detecting **prostate cancer** in the patient;

(11) a method for monitoring the progression of **prostate cancer** in a patient comprising:

(a) step (a) as defined in (10);

(b) determining in the sample an amount of a protein or polypeptide that binds to the binding agent;

(c) repeating steps (a) and (b); and

(d) comparing the amount of polypeptide detected in (b) and (c) to monitor the progression of **prostate cancer** in the patient; and

(12) another method for detecting **prostate cancer** in a patient comprising:

(a) contacting a biological sample from a patient with at least 2 **oligonucleotide** (ON) primers in a **PCR**, where at least one of the ON primers is specific for a DNA molecule selected from sequences N1-N7 and N14-N37 defined in the specification; and

(b) detecting in the sample a DNA sequence that amplifies in the presence of the ON primer, thereby detecting **prostate cancer**.

USE - The polypeptides and DNA obtained from prostate tumor cells and antibodies can be used in the treatment, diagnosis and monitoring of **prostate cancer**.

Dwg.0/3

L31 ANSWER 20 OF 48 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1999-229540 [19] WPIDS
AB WO 9914340 A UPAB: 19990518

NOVELTY - New substantially purified human PRL-1 phosphatase (I) (HPRL-1) has a 457 amino acid sequence given in the specification.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a substantially purified variant of (I), having at least 90% identity to (I), and retaining at least one functional characteristic of the PRL-1 gene product;

(2) an isolated and purified **polynucleotide** (II) encoding (I), and **polynucleotide** fragments;

(3) a **polynucleotide** sequence which **hybridizes** or is complementary to (II);

(4) an expression vector containing (II);

(5) a host cell containing the vector;

(6) preparation of (I);

(7) an antibody specific for (I); and

(8) purified agonists and antagonists of (I)

USE - PRL-1 polypeptide (I) and **polynucleotide** (II) are useful for diagnosis and in compositions for treatment of disorders associated with expression levels of PRL-1, and PRL-1 antagonists are useful for treatment of disorders associated with cell proliferation, especially cancer and immune disorders (claimed) e.g. bone, skin, testicular and **prostate cancer**, and AIDS, Chron's disease, multiple sclerosis, osteoporosis and allergies.

PRL-1 **polynucleotide** (II) is also useful for detecting PRL-1 **polynucleotides** in a sample due to overexpression of the gene, by **hybridization**, preferably to nucleic acid which has been **PCR** amplified. It is useful for diagnosis, prevention and treatment of disorders associated with cell proliferation. It is also useful for producing antibodies, which are useful for diagnosis of the above conditions, and for monitoring treatment, and for screening for antagonists (potential drugs).

The vector is useful in gene therapy by delivering PRL-1 **polynucleotides**/protein to a subject for treatment of the above immune disorders and cancer.

Dwg.0/10

L31 ANSWER 21 OF 48 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1999-610253 [52] WPIDS
AB US 5972684 A UPAB: 19991210

NOVELTY - An isolated and purified **polynucleotide** sequence (I) encoding human carbonic anhydrase VIII (CAVIII) (which has a defined 328 amino acid sequence given in the specification), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(i) an isolated and purified **polynucleotide** sequence (I')

which is fully complementary to (I);

(ii) an expression vector (Iv) comprising (I);

(iii) a host cell (Ic) comprising (Iv);

(iv) a method (X) for producing a CAVIII polypeptide, comprising:

(1) culturing (Ic) to express the polypeptide; and

(2) recovering the polypeptide from the host cell culture; and

(v) a method for detecting nucleic acids encoding CAVIII in samples, comprising:

(1) **hybridizing** (I') the nucleic acids in the sample to form **hybridization** complexes; and

(2) detecting the **hybridization** complexes produced (the presence of a **hybridization** complex correlates with the presence of CAVIII nucleic acids in the sample).

ACTIVITY - Cytostatic; nootropic; anti-parkinsonian disease; cerebroprotective; neuroprotective; vasotropic; hypotensive; ophthalmological; anti-arthritic; anti-diabetic; anti-allergic; anti-asthmatic; anti-inflammatory; anti-AIDS; immunomodulatory.

No relevant biological data given.

MECHANISM OF ACTION - Gene therapy, (I) (or vectors comprising (I) (Iv)) may be administered to rectify mutations or deletions in a patient's genome that affect the activity of CAVIII by expressing inactive proteins or to supplement the patients own production of CAVIII polypeptides.

USE - (I) and the protein it encodes may be used in the diagnosis, prevention and treatment of circulatory and neuronal diseases, inflammation and cancers. For example, (I) (and vectors containing (I) (Iv)) and the CAVIII polypeptide may be administered to treat disorders associated with decreased CAVIII expression or inhibition of its activity which results in inflammation. Inflammation may (for example) be associated with disorders such as acquired immune deficiency syndrome (AIDS), bronchitis, asthma, allergies, diabetes mellitus and rheumatoid arthritis. (I), (Iv) and/or CAVIII may also be administered to treat circulatory disorders of the vascular or lymph system (e.g. hypertension, glaucoma and shock) associated with decreased CAVIII expression and activity. (I) or (Iv) may be administered to treat any of the above diseases by rectifying mutations or deletions in a patient's genome that affect the activity of CAVIII by expressing inactive proteins or to supplement the patients own production of CAVIII polypeptides. Conversely, antisense nucleic acid molecules (I') may be administered to down regulate CAVIII expression by binding with the cells own CAVIII genes and preventing their expression.

(I) and (I') may also be used as DNA probes in diagnostic assays (e.g. **polymerase chain reactions** (**PCR**)) to detect and quantitate the presence of similar nucleic acid sequences in samples, and hence which patients may be in need of restorative therapy.

They may also be used to study the expression and function of CAVIII polypeptides and their role in cellular metabolism.

Additionally, (I) may be used to produce CAVIII enzymes, according to standard recombinant DNA methodology (for example see Sambrook et al., Molecular Biology: A Laboratory Manual, (1989)), by inserting the nucleic acids into a host cell (Ic) and culturing the cell to express the protein.

The CAVIII polypeptides may then be used as antigens in the production of antibodies against CAVIII and in assays to identify modulators (agonists and antagonists) of CAVIII expression and activity. The anti-CAVIII antibodies and CAVIII antagonists may also be used to down

regulate CAVIII expression and activity. They may be used in this way to treat disorders associated with increased CAVIII expression or enhancement of its activity which results in inflammation. As above, inflammation may (for example) be associated with disorders such as acquired immune deficiency syndrome (AIDS), bronchitis, asthma, allergies, diabetes mellitus and rheumatoid arthritis. These inhibitors may also be used to treat circulatory disorders of the vascular or lymph system (e.g. hypertension, glaucoma and shock) associated with increased CAVIII expression and activity. Antagonists of CAVIII may also be used to treat neuronal disorders (e.g. Parkinson's disease, Alzheimer's disease and Down's syndrome) and cancers (e.g. leukemia, melanomas and **prostate cancer**).
Dwg.0/3

L31 ANSWER 22 OF 48 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1999-610249 [52] WPIDS
AB US 5972660 A UPAB: 19991210
NOVELTY - An isolated and purified **polynucleotide** sequence (I) encoding a human hydroxypyruvate reductase (hHPR) enzyme (which has a defined 328 amino acid sequence given in the specification), is new.
DETAILED DESCRIPTION - An isolated and purified **polynucleotide** sequence (I) encoding a human hydroxypyruvate reductase (hHPR) enzyme (which has a defined 328 amino acid sequence given in the specification), is new. hHPR is part of the glycolate pathway and catalyses the conversion of hydroxypyruvate to glycerate with the oxidation of reduced nicotinamide adenine dinucleotide (NADH) and nicotinamide adenine dinucleotide phosphate (NADPH). hHPR recycles nucleotides and bases back into pathways leading to the synthesis of adenine triphosphate (ATP) and guanine triphosphate (GTP). ATP and GTP are used to produce DNA and RNA and to control various aspects of signal transduction and energy metabolism.
INDEPENDENT CLAIMS are also included for the following:
(i) an isolated and purified **polynucleotide** (I') completely complementary to (I);
(ii) an expression vector (Iv) comprising (I);
(iii) a host cell (Ihc) comprising (Iv);
(iv) a method (X) for producing hHPR, comprising:
(1) culturing (Ihc) to express the polypeptide; and
(2) recovering the polypeptide from the host cell culture; and
(v) a method (Y) for detecting nucleic acids encoding hHPR in a sample, comprising:
(1) **hybridizing** (I') to nucleic acids within the sample for 16 hours at 40 deg. C to form a **hybridization** complex and washing at room temperature under increasingly stringent conditions up to 0.1 multiply saline sodium citrate and 0.5% sodium dodecyl sulfate; and
(2) detecting the **hybridization** complex (the presence of the complex is indicative of the presence of nucleic acids encoding hHPR in the sample).
USE - (I) and the protein it encodes may be used in the diagnosis, prevention and treatment of disorders associated with cell proliferation, cancers and immune responses. For example, (I) (and vectors containing (I) (Iv)) and the polypeptide it encodes may be used to treat disorders associated with inappropriate or reduced hHPR expression by rectifying mutations or deletions in a patient's genome that affect the activity of hHPR by expressing inactive proteins or to supplement the patients own production of the polypeptide. Conversely, antisense nucleic acid molecules (I') may be administered to down regulate hHPR expression by

binding with the cells own hHPR genes and preventing their expression.

(I) and (I') may also be used as DNA probes in diagnostic assays (e.g. **polymerase chain reactions** (**PCR**)) to detect and quantitate the presence of similar nucleic acid sequences in samples, and hence which patients may be in need of restorative therapy.

They may also be used to study the expression and function of hHPR polypeptides and their role in cellular metabolism.

Additionally, (I) may be used to produce hHPR, according to standard recombinant DNA methodology (for example see Sambrook et al., Molecular Biology: A Laboratory Manual, (1989)), by inserting the nucleic acids into a host cell (Ic) and culturing the cell to express the protein.

The hHPR polypeptides may then be used as antigens in the production of antibodies against hHPR and in assays to identify modulators (agonists and antagonists) of hHPR expression and activity. The anti-hHPR antibodies and hHPR antagonists may also be used to down regulate hHPR expression and activity. They may be used in this way to treat immune disorders (e.g. acquired immune deficiency syndrome (AIDS), anemia, asthma, atherosclerosis, multiple sclerosis, allergies and osteoarthritis and viral infections) and cancers (e.g. **prostate cancer**, lung cancer, leukemia and melanomas).

Dwg.0/3

L31 ANSWER 23 OF 48 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1999-632430 [54] WPIDS
CR 2000-181798 [16]
AB US 5965369 A UPAB: 20000330

NOVELTY - Isolated nucleic acids ((I) and (II)) encoding the human succinyl-coenzyme A synthetase holoenzymes (SCSH)-1 and SCSH-2 (respectively), are new. SCSH-1 and SCSH-2 have defined 346 and 432 (respectively) amino acid sequences given in the specification.

DETAILED DESCRIPTION - SCS is a component of the tricarboxylic acid cycle (TCA cycle) which catalyses the formation of succinate from succinyl-coenzyme A (CoA) and the formation of guanine triphosphate (GTP) from guanine diphosphate (GDP) and phosphate within the mitochondrial matrix. SCS activity has also been found to be involved in a number of amino acid metabolic pathways (e.g. valine and methionine are catabolized in a series of enzyme catalyzed reactions to form succinyl-CoA).

INDEPENDENT CLAIMS are also included for the following:

(i) isolated **polynucleotides** ((I') and (II')) which **hybridize** to (I) and (II) (respectively) under stringent conditions;

(ii) expression vectors ((Iv) and (IIv) comprising (I) and (II) (respectively);

(iii) host cells ((Ihc) and (IIhc)) comprising (Iv) and (IIv) (respectively);

(iv) a method (X) for producing SCSH-1 and/or SCSH-2, comprising:

(1) culturing (Ihc) and/or (IIhc) to express the polypeptide; and

(2) recovering the polypeptides from the host cell culture; and

(v) a method (Y) for detecting (I) and/or (II) in sample, comprising:

(1) **hybridizing** (I') and/or (II') to the nucleic acids in the sample to form a **hybridization** complex; and

(2) detecting the presence of **hybridization** complexes (the presence of **hybridization** complexes correlates with the presence of (I) and/or (II) in the sample).

ACTIVITY - Cytostatic; anti-cancer; anti-fertility; immunomodulatory;

neuroactive; anti-Parkinson's; anti-Alzheimer's; neuroprotective; nootropic; anti-goiter; anti-Cushing's; anti-asthmatic; anti-acquired immune deficiency syndrome (AIDS).

No relevant biological data given.

MECHANISM OF ACTION - Gene therapy, (I), (II) or vectors containing (I) and (II) (i.e. (Iv) and (IIv)) may be administered to treat any of the above diseases by rectifying mutations or deletions in a patient's genome that affect processes associated with the tricarboxylic acid cycle (TCA cycle), vesicle trafficking and amino acid catabolism by expressing inactive proteins or to supplement the patients own production of SCSH-1 and SCSH-2.

USE - (I), (II) and the proteins they encode may be used in the diagnosis, prevention and treatment of disorders associated with the inappropriate expression and activity of SCS. For example, they may be used to treat neoplastic (e.g. leukemia, melanoma and **prostate cancer**), reproductive (e.g. polycystic ovary syndrome, infertility and disruptions of spermatogenesis), immunological (e.g. Addison's disease, acquired immune deficiency syndrome (AIDS) and asthma), vesicle trafficking (e.g. glucose-galactose malabsorption syndrome, goiter and Cushing's disease) and nervous disorders (e.g. Alzheimer's disease, Parkinson's disease and Creutzfeldt-Jakob disease).

(I), (II) or vectors containing (I) and (II) (i.e. (Iv) and (IIv)) may be administered to treat any of the above diseases by rectifying mutations or deletions in a patient's genome that affect processes associated with the tricarboxylic acid cycle (TCA cycle), vesicle trafficking and amino acid catabolism by expressing inactive proteins or to supplement the patients own production of SCSH-1 and SCSH-2. Conversely, antisense nucleic acid molecules (i.e. (I') and (II')) may be administered to down regulate SCSH-1 and SCSH-2 protein expression by binding with the cells own SCS genes and preventing their expression.

(I), (II), (I') and (II') may also be used as DNA probes in diagnostic assays (e.g. **polymerase chain reactions** (**PCR**)) to detect and quantitate the presence of similar nucleic acid sequences in samples, and hence which patients may be in need of restorative therapy.

They may also be used to study the expression and function of SCS proteins and their role in the TCA cycle and amino acid catabolism.

Additionally, (I) and (II) may be used to produce SCSH-1 and SCSH-2 (respectively) according to standard recombinant DNA methodologies (for example see Sambrook et al., Molecular Biology: A Laboratory Manual, (1989)), by inserting the nucleic acids into a host cell (i.e. (Ihc) and (IIhc) and culturing the cells to express the proteins.

The SCSH-1 and SCSH-2 proteins may then be used as antigens in the production of antibodies to SCS and in assays to identify modulators of SCSH-1 and SCSH-2 expression and activity. These antagonists may then be used to increase or decrease SCS activity.

Dwg.0/2

L31 ANSWER 24 OF 48 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1999-508170 [42] WPIDS
AB US 5945289 A UPAB: 19991014

NOVELTY - Screening for **prostate cancer** in a patient comprising genotyping at apolipoprotein E (ApoE) alleles, a genotype of ApoE4/ApoE4 indicating an increased propensity for **prostate cancer**.

USE - The new method is useful for assessing if a patient has an enhanced predisposition to **prostate cancer** (claimed). The method can also be used to stage **prostate cancer** and predict prognosis.

35 men with **prostate cancer** tested for the ApoE4 allele had a frequency of 24 %, compared to the general male population of 12 %.

ADVANTAGE - Prior art methods for detection of **prostate cancer** still require invasive biopsies, so the new method is less intrusive than these methods.

Dwg.0/0

L31 ANSWER 25 OF 48 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1999-443600 [37] WPIDS
AB US 5932475 A UPAB: 19990914

NOVELTY - An isolated and purified **polynucleotide** sequence (I) encoding a human nucleolin-like peptide (designated HNLP) (HNLP is the main protein component in the nucleolus of eukaryotic cells and is an essential part of ribosome biosynthesis and also plays an important role in importing proteins to the nucleus), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(i) a composition comprising (I);

(ii) an **oligonucleotide** sequence (II) complementary to (I) (i.e. an anti-sense molecule);

(iii) an expression vector (III) comprising (I) (or a fragment of (I));

(iv) a host cell (IV) containing (III);

(v) a method (X) for producing the HNLP protein, comprising:

(1) culturing the host cell (IV) under conditions suitable for expression of the polypeptide; and

(2) recovering the polypeptide from the host cell culture; and

(vi) a method (Y) for detecting a **polynucleotide** encoding the HNLP peptide in a sample containing nucleic acids, comprising **hybridizing** (II) to the nucleic acids in the sample; and detecting the presence of **hybridization** complexes (the presence of complexes indicates the presence of (I) in the sample).

ACTIVITY - Anticancer; Immunosuppressive

MECHANISM OF ACTION - None given.

USE - (I) and the protein it encodes may be used in the diagnosis, prevention and treatment of disorders associated with abnormal expression of HNLP. For example, they may be used to treat cancers (e.g. melanoma, breast cancer and **prostate cancer**), autoimmune disorders (e.g. autoimmune hemolytic anemia and inflammatory bowel disease) and, in particular, Alzheimer's disease.

They may also be used to study the function of the HNLP peptides, the formation (biosynthesis) of ribosomes and the intake of proteins into the nucleus.

In particular, (I) may be used to produce the HNLP protein, according to standard recombinant DNA methodology, by inserting the **oligonucleotide** into a host cell (i.e. (IV)) and culturing the cell to express the protein. The HNLP protein may then be used as an antigen in the production of antibodies. (I) or vectors containing (I) (i.e. (III)) may be administered to treat any of the above diseases by rectifying mutations or deletions in a patient's genome that affect the activity of HNLP. The HNLP protein itself may be used to assay for inhibitors (including antibodies which modulate the activity of HNLP).

Conversely, anti-sense nucleic acid molecules (i.e. (II)) may be administered to down regulate HNLP expression by binding with the patient's own HNLP genes and preventing their expression ((II) may be used in this way to treat and counter over expression of HNLP proteins as

occurs in a number of cancers.
(I) may also be used as DNA probes in diagnostic assays (e.g. **polymerase chain reactions** (**PCR**)) to detect and quantitate the presence of similar nucleic acid sequences in samples, and hence which patients may be in need of restorative therapy.
Dwg.0/0

L31 ANSWER 26 OF 48 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1999-394623 [33] WPIDS
AB US 5919661 A UPAB: 19990819
NOVELTY - An isolated and purified **polynucleotide** (I) encoding cytokine inducible regulatory protein-1 (CIRP-1) (307 amino acid protein), is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) an expression vector containing (I);
(2) a host cell containing the vector of (1);
(3) a method for producing (II) comprising culturing the host cell of (2) and recovering the polypeptide;
(4) an isolated **polynucleotide** which **hybridizes** under stringent conditions to (I); and
(5) an isolated and purified **polynucleotide** which is completely complementary to (I).
USE - **Polynucleotide** sequences encoding CIRP-1 may be used for the diagnosis of cancers including adenocarcinoma, leukemia, breast cancer, **prostate cancer** and diagnosis of immune responses associated with AIDS, bronchitis, diabetes mellitus, multiple sclerosis and osteoporosis. **Polynucleotide** sequences encoding CIRP-1 may also be used in Southern or Northern analysis, dot blot, or other membrane-based technologies; in **PCR**; or in dipstick, pin, ELISA assays or microarrays utilizing fluids or tissues from patient biopsies to detect altered CIRP-1 expression.
Dwg.0/3

L31 ANSWER 27 OF 48 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1999-394618 [33] WPIDS
AB US 5919627 A UPAB: 19990819
NOVELTY - An isolated and purified **polynucleotide** sequence (I) (660 bp) encoding human microsomal glutathione-S-transferase (MGST) (II) (152 amino acid protein), is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a **polynucleotide** sequence which **hybridizes** to (I) under stringent conditions;
(2) a **polynucleotide** sequence completely complementary to (I);
(3) an expression vector containing the **polynucleotide** sequence of (I);
(4) a host cell containing the vector of (3);
(5) a method of producing (II) comprising culturing the host cell of (4) and recovering the polypeptide; and
(6) a method of detecting (I) comprising:
(a) **hybridizing** the **polynucleotide** of (2) to nucleic acid of a biological sample and forming a **hybridization** complex; and
(b) detecting the **hybridization** complex, where its presence correlates with the presence of (I).
USE - **Polynucleotide** sequences encoding MGST may be used for the diagnosis of cancers including adenocarcinoma, leukemia, breast

cancer, **prostate cancer** and diagnosis of immune responses associated with AIDS, bronchitis, diabetes mellitus, multiple sclerosis and osteoporosis. **Polynucleotide** sequences encoding MGST may also be used in Southern or Northern analysis, dot blot, or other membrane-based technologies; in **PCR**; or in dipstick, pin, ELISA assays or microarrays utilizing fluids or tissues from patient biopsies to detect altered MGST expression.
Dwg.0/3

L31 ANSWER 28 OF 48 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1999-228548 [19] WPIDS
AB . US 5885834 A UPAB: 19990518
NOVELTY - Antisense oligodeoxynucleotides (AS-ODN(s)) which will bind to mRNA encoding phosphodiesterase PDE1B1 enzymes and their use in inducing programmed cell death (apoptosis) in cancer cells, are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for: (i) a method (X) of inducing programmed cell death in cancer cells which comprises: (1) identifying the phosphodiesterase enzyme PDE1B1 in a cell line containing the cancer cells; (2) synthesising an AS-ODN inhibitor which will bind to mRNA encoding PDE1B1; and (3) applying the AS-ODN to the cell line to inhibit the enzymatic activity of the PDE1B1 and induce apoptosis in the cells; (ii) a purified and isolated **polynucleotide** (I) encoding a 63 kDa calmodulin-dependent phosphodiesterase PDE1B1 enzyme from a human leukemic lymphoblastoid cell line; and (iii) an AS-ODN (asI) which will bind to mRNA encoding phosphodiesterase PDE1B1 enzymes.

ACTIVITY - Cytostatic; Apoptotic

MECHANISM OF ACTION - AS-ODNs inhibit the expression of a protein by two mechanisms: (i) by degradation of RNA by the ubiquitous enzyme RNase H, which selectively cleaves the RNA of DNA-RNA heteroduplexes; and (ii) the arrest of translation initiation caused by AS-ODN **hybridization** to the 5' un-translated region or the translation initiation site on the mRNA. Inhibition of phosphodiesterase (PDE) enzyme expression results in elevated levels of cAMP in the cells due to PDE1B1 being involved in the metabolism of cAMP. The elevated cAMP levels result in apoptosis by inhibition of DNA synthesis.

RPMI 8392 cells were studied for the presence of PDE1B1 mRNA using quantitive Reverse Transcription **Polymerase Chain Reaction** (RT-**PCR**) with primers specific for PDE1B1 DNA. It was found that the level PDE1B1 mRNA was diminished after 1 day in cells treated with 10-30 mu M AS-ODN, and undetectable after 2 days. Experiments were conducted to determine if inhibition of the expression of the gene for PDE1B1 could induce apoptosis. Based on the nucleotide (nt) sequence obtained for PDE1B1 from RPMI 8392 cells, an 18 nt phosphorothioate antisense oligodeoxynucleotide (PS-ODN) was synthesized starting from 6 nt to the 5'-end of the translation initiation codon and extending over the first 4 codons of the Open Reading Frame (ORF). As a control, a nonsense oligodeoxynucleotide (NS-ODN) containing the same base composition, but in a random, scrambled order, was also synthesized. These synthetic phosphorothioate ODNs were added to RPMI 8392 cells in concentrations from 0.3-30 mM and the cells were examined for apoptosis. DNA isolated from RPAR 8392 cells was analyzed for fragmentation on 2% agarose gels after the cells were cultured with different concentrations of phosphorothioate antisense (AS) or phosphorothioate nonsense (NS) ODN for 2 days or 1, 2 and 3 days. Cell culture was done at a concentration of

about 106/ml in 1 ml volumes in 24 well plates, in RPMI 1640 growth medium-L except that the fetal calf serum was heat inactivated at 65 0C for 1 hour (hr) to help minimize nuclease activity. The sequence of the 18 nt AS-ODN used was 5'-GGACAGCFCCATGCTCAG-3', and the sequence of the 18 nt NS-ODN used was 5'-TACGTGAGGCACCTACGC-3'. Controls (lane 2 in all gels) represent no additions of ODN to the cells. Markers (lane 1 in all gels) are Hae III digests of fX174 DNA from GIIBCO/BRL. 48 hr treatment with 30 mM AS-ODN clearly induced apoptosis in these cells, whereas 30 mM NS-ODN did not. When cells were examined for apoptosis at 1, 2. and 3 days after addition of AS and NS-ODNS, it was found that after 3 days, AS-ODN induced apoptosis at both 10 mM and 30 mM, whereas in all cases, NS-ODN had no effect.

USE - The method (X) and AS-ODN (asI) are useful in inducing cAMP stimulated apoptosis and may be in the treatment of immunoproliferative disorders and immune disfunctions such as acute lympholytic leukemia, breast and **prostate cancer.**

ADVANTAGE - It is known that increasing cellular cAMP levels can lead to cell death and the use of cAMP analogues or agents which increase cAMP content has been suggested as a method of treating cancers by inducing apoptosis. However cAMP has profound side effects on the metabolic machinery, growth regulation and transcription in most cells. Indiscriminate elevation of cAMP throughout the body would probably produce a wide range of side effects. The antisense oligodeoxynucleotide (AS-ODN) (asI) is capable of selectively inhibiting the expression of a specific isoform of the PDE enzyme (PDE1B1) to cause an increase in the cell cAMP content and apoptosis in cancer tissue. (asI) is selective because PDE1B1 is only expressed in cancerous cells, therefore the use of (I) avoids the adverse effect associated with a systemic increase in cAMP levels. In particular, the use of AS-ODNs is unlikely to affect brain function as AS-ODNs distribute poorly into the brain tissue.

Dwg.0/0

L31 ANSWER 29 OF 48 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1999-214055 [18] WPIDS
AB US 5882864 A UPAB: 19990511

NOVELTY - Methods for diagnosing **prostate cancer** or benign prostatic hyperplasia cells in a biological sample using **oligonucleotide** probes ((I)-(XXIV) specific for marker genes associated with tumor differentiation and progression in Reverse Transcription **Polymerase Chain Reaction** analysis, are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for: (i) a method (MethI) for detecting **prostate cancer** or benign prostatic hyperplasia cells in a biological sample, which comprises: (1) extracting nucleic acids from the sample; (2) amplifying the nucleic acids by **Polymerase Chain Reaction (PCR)** to form amplification products (aps); (3) contacting the aps with **oligonucleotide** probes which will **hybridize** under stringent conditions to the isolated nucleic acid sequences ((I) to (XXIV)); (4) detecting the aps that **hybridize** with the probes; and (5) quantifying the amount of aps that **hybridize** with the probes; and (ii) a method (MethII) for detecting **prostate cancer** or benign prostatic hyperplasia cells in a biological sample, which comprises: (1) extracting nucleic acids from the sample; (2) providing primers that will selectively amplify the isolated nucleic acid sequences (I) to (XXIV); (3) Amplifying the nucleic acids with the primers

by **PCR** to form aps; (4) detecting the nucleic acid aps; and (5) quantifying the amount of aps formed.

USE - (MethI) and (MethII) are diagnostic techniques useful for detecting and monitoring the progression of benign prostatic hyperplasia and human **prostate cancer** (the most prevalent form of cancer and a major cause of death in males) prior to the tumor undergoing metastasis, therefore allowing the optimal method of treatment to be determined before the condition becomes life threatening.

DESCRIPTION OF DRAWING(S) - The graph displays normalized quantitative Reverse Transcription **Polymerase Chain Reaction** (RT-**PCR**) analysis for the full length Her2/neu which shows that it is over expressed in prostate tumors compared to normal prostate cells and benign prostatic hyperplasia. N= normal prostate, B= benign prostatic hyperplasia (BPH), NB= needle core biopsy of **prostate cancer**, T= primary **prostate cancer**, LM= metastatic lymph node **prostate cancer**, NC= negative control.

Dwg.10/15

L31 ANSWER 30 OF 48 MEDLINE DUPLICATE 3

2000005547 Document Number: 20005547. The luteinizing hormone-releasing hormone receptor in human **prostate cancer** cells: messenger ribonucleic acid expression, molecular size, and signal transduction pathway. Limonta P; Moretti R M; Marelli M M; Dondi D; Parenti M; Motta M. (Center for Endocrinological Oncology, Department of Endocrinology, University of Milano, Italy.. limonta@mailserver.unimi.it) . ENDOCRINOLOGY, (1999 Nov) 140 (11) 5250-6. Journal code: EGZ. ISSN: 0013-7227. Pub. country: United States. Language: English.

AB Evidence has accumulated indicating that LHRH might behave as an autocrine/paracrine growth inhibitory factor in some peripheral tumors. However, LHRH receptors in tumor cells have not been fully characterized, so far. The present experiments were performed to analyze: 1) the messenger RNA expression; 2) the molecular size; and 3) the signal transduction pathway of LHRH receptors in **prostate cancer**. For these studies, the human androgen-dependent LNCaP and androgen-independent DU 145 **prostate cancer** cell lines were used. 1) By RT-**PCR**, a complementary DNA product, which **hybridized** with a 32P-labeled **oligonucleotide** probe specific for the pituitary LHRH receptor complementary DNA, was found both in LNCaP and in DU 145 cells. 2) Western blot analysis, using a monoclonal antibody raised against the human pituitary LHRH receptor, revealed the presence of a protein band of approximately 64 kDa (corresponding to the molecular mass of the pituitary receptor) in both cell lines. 3) In LNCaP and DU 145 cells, pertussis toxin completely abrogated the antiproliferative action of a LHRH agonist (LHRH-A). Moreover, LHRH-A substantially antagonized the pertussis toxin-catalyzed ADP-ribosylation of a Galpha(i) protein. Finally, LHRH-A significantly counteracted the forskolin-induced increase of intracellular cAMP levels in both cell lines. These data demonstrate that the LHRH receptor, which is present in **prostate cancer** cells, independently of whether they are androgen-dependent or not, corresponds to the pituitary receptor, in terms of messenger RNA expression and protein molecular size. However, at variance with the receptor of the gonadotrophs, **prostate cancer** LHRH receptor seems to be coupled to the Galpha(i) protein-cAMP signal transduction pathway, rather than to the Galpha(q/11)-phospholipase C signaling system. This might be responsible for the different actions of LHRH in anterior pituitary and in

prostate cancer.

L31 ANSWER 31 OF 48 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 4
1998:344536 Document No. 129:51704 Detection of metastatic **prostate cancer** based on the prostate-specific glandular kallikrein hK2 protein or nucleic acid. Tindall, Donald J.; Young, Charles Y. F.; McCormick, Daniel J.; Klee, George G.; Saedi, Mohammad Saeed; Kumar, Abhay; Rittenhouse, Harry G.; Wolfert, Robert L. (Mayo Foundation for Medical Education and Research, USA; Hybritech Incorporated). PCT Int. Appl. WO 9821365 A2 19980522, 106 pp. DESIGNATED STATES: W: AU, CA, CN, JP, MX; RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1997-US20948 19971114. PRIORITY: US 1996-759354 19961114.
AB **Prostate cancer** is detected by detg. the presence of prostate-specific glandular Kallikrein hK2 polypeptide or hK2 RNA in a physiol. sample. The method comprises contacting cDNA obtained by reverse transcription of RNA from a human sample with hK2-specific **oligonucleotide** primers so as to yield amplified hK2 DNA. The presence of the amplified hK2 DNA is then detected. The presence of amplified hK2 DNA in blood cells, after RT-**PCR**, is correlated with **prostate cancer**, ie., 67% of **prostate cancer** patients express hK2, 17% express prostate-specific antigen (PSA), and 17% express both hK2 and PSA. The hK2 protein may also be detected by immunoassay. Nucleotide sequence and deduced amino acid sequences are also provided for human hK2 cDNA and its encoded mature, pro-, and prepro-hK2 proteins.

L31 ANSWER 32 OF 48 CAPLUS COPYRIGHT 2000 ACS
1998:761987 Document No. 130:21376 PS116 protein and its cDNA sequence useful for detecting diseases of the prostate in humans. Billing-Medel, Patricia A.; Cohen, Maurice; Colpitts, Tracey L.; Friedman, Paula N.; Gordon, Julian; Granados, Edward N.; Hodges, Steven C.; Klass, Michael R.; Kratochvil, Jon D.; Roberts-Rapp, Lisa; Russell, John C.; Stroupe, Stephen D. (Abbott Laboratories, USA). PCT Int. Appl. WO 9851805 A1 19981119, 118 pp. DESIGNATED STATES: W: CA, JP; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US10041 19980515. PRIORITY: US 1997-856653 19970515.
AB A set of contiguous and partially overlapping cDNA sequences and polypeptides encoded thereby, designated as PS116 and transcribed from human prostate tissue, is described. The full-length consensus cDNA sequence contains an open reading frame encoding a protein 123 amino acids in length with some homol. to chicken stem cell antigen SCA2. These sequences are useful for the detecting, diagnosing, staging, monitoring, prognosticating, in vivo imaging, preventing or treating, or detg. the predisposition of an individual to diseases and conditions of the prostate, such as **prostate cancer**. Also provided are antibodies which specifically bind to PS116-encoded polypeptide or protein, and agonists or inhibitors which prevent action of the tissue-specific PS116 polypeptide, which mols. are useful for the therapeutic treatment of prostate diseases, tumors or metastases.

L31 ANSWER 33 OF 48 CAPLUS COPYRIGHT 2000 ACS
1998:388623 Document No. 129:50533 Cloning of human glutathione S-transferase and its diagnostic and therapeutic uses. Goli, Surya K.; Hillman, Jennifer L. (Incyte Pharmaceuticals, Inc., USA; Goli, Surya K.;

Hillman, Jennifer L.). PCT Int. Appl. WO 9823758 A1 19980604, 73 pp. DESIGNATED STATES: W: AT, AU, BR, CA, CH, CN, DE, DK, ES, FI, GB, IL, JP, KR, MX, NO, NZ, RU, SE, SG, US, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1997-US21243 19971119. PRIORITY: US 1996-756771 19961126.

AB The present invention provides a human glutathione s-transferase (HGST) and **polynucleotides** which identify and encode HGST. Nucleic acids encoding human HGST were first identified in Incyte clone 1553079 from a bladder tumor cDNA library; a consensus sequence was derived from overlapping and/or extended nucleic acid sequences. HGST is 222 amino acids in length and is characterized as having similarity to Alpha class GSTs from normal liver, pGHTH2, human hepatoma A1.1, and mouse lung GST 5.7. In addn. to bladder tumor, partial transcripts of the cDNA encoding HGST are found in fetal tissues (kidney and pancreas) and in prostate tissue adjacent to **prostate cancer**. The invention also provides genetically engineered expression vectors and host cells comprising the nucleic acid sequences encoding HGST and a method for producing HGST. The invention also provides for agonists, antibodies, or antagonists specifically binding HGST, and their use, in the prevention and treatment of cancer and other diseases assocd. with the expression of HGST. Addnl., the invention provides for the use of antisense mols. to **polynucleotides** encoding HGST for the treatment of cancer and other diseases assocd. with the expression of HGST. The invention also provides diagnostic assays which utilize the **polynucleotide**, or fragments or the complement thereof, and antibodies specifically binding HGST.

L31 ANSWER 34 OF 48 CAPLUS COPYRIGHT 2000 ACS

1998:106004 Document No. 128:176923 Biomarkers and targets for diagnosis, prognosis and management of prostate disease. Veltri, Robert; O'Hara, S. Mark; An, Gang; Ralph, David (Urocor, Inc., USA). PCT Int. Appl. WO 9804689 A1 19980205, 230 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1996-US12516 19960731.

AB Disclosed are diagnostic techniques for the detection of human **prostate cancer**. Genetic probes and methods useful in monitoring the progression and diagnosis of **prostate cancer** are described. The invention relates particularly to probes and methods for evaluating the presence of RNA species that are differentially expressed in **prostate cancer** compared to normal human prostate or benign prostatic hyperplasia. Thus, 26 markers of prostate disease were identified by RNA fingerprinting or quant. RT-**PCR**. These include 20 previously unknown gene products, as well as nucleic acid products of the .alpha.6-integrin, prostatic acid phosphatase, fibronectin, and cyclin A genes and a truncated nucleic acid product of the Her2-neu gene, which have been identified in other forms of cancer but not in **prostate cancer**.

L31 ANSWER 35 OF 48 CAPLUS COPYRIGHT 2000 ACS

1997:684152 Document No. 127:327442 Nucleic acid primers for detecting micrometastasis of **prostate cancer**. Croce, Carlo; Gomella, Leonard; Mulholland, S. Grant; Moreno, Jose G.; Fischer, Rainer

(Thomas Jefferson University, USA). U.S. US 5674682 A 19971007, 18 pp. Cont.-in-part of U.S. 5,506,106. (English). CODEN: USXXAM.
APPLICATION:
US 1994-358782 19941215. PRIORITY: US 1992-973322 19921029; US 1994-294611 19940823.
AB **Oligonucleotides** for and a method of diagnosing prostate micrometastasis are provided by the present invention whereby nucleic acids from a tissue sample from a patient are isolated, nucleic acids from the tissue sample specific for **prostate cancer** are amplified, or a signal generated by **hybridization** of a probe specific to a **prostate cancer** specific nucleic acid is amplified; and detection of amplified nucleic acids is indicative of micrometastasis of **prostate cancer**. PSA-specific **PCR** primers were used to examine RNA isolated from blood of 12 **prostate cancer** patients and 17 control patients. Of the 12 prostatic adenocarcinoma patients with metastatic disease, 4 cases (2 stage D1, one stage D2, and one stage D3) had pos. PSA signals indicating presence of prostatic epithelial cells in the peripheral venous blood. The 17 neg. controls consisted of 8 women and 9 men with benign prostatic hyperplasia.

L31 ANSWER 36 OF 48 MEDLINE
96375799 Document Number: 96375799. Bombesin specifically induces intracellular calcium mobilization via gastrin-releasing peptide receptors in human **prostate cancer** cells. Aprikian A G; Han K; Chevalier S; Bazinet M; Viallet J. (Department of Surgery (Urology), McGill University, Montreal, Quebec, Canada.) JOURNAL OF MOLECULAR ENDOCRINOLOGY, (1996 Jun) 16 (3) 297-306. Journal code: AEG. ISSN: 0952-5041. Pub. country: ENGLAND: United Kingdom. Language: English.
AB Bombesin and gastrin-releasing peptide (GRP) are potent neuropeptides expressed by **prostate cancer** neuroendocrine cells and are related to the progression of this malignancy. This study characterizes bombesin receptors in human **prostate cancer** cell lines (PC-3, DU-145, LNCaP) and assesses the in vitro effect of bombesin on signal transduction and cell proliferation. [125I]Tyr4-bombesin binding assays (37 degrees C) and Scatchard analyses revealed the presence of a single class of high-affinity receptors with similar Kd values (1.5, 1.1 and 3.6 x 10(-10) M in PC-3, DU-145 and LNCaP cells respectively) but with significant differences in the number of binding sites per cell (47.6, 1.5 and 0.1 x 10(3) in PC-3, DU-145 and LNCaP cells respectively). Molecular characterization of the binding sites performed in PC-3 cells by cross-linking experiments and SDS/PAGE revealed a single radioactive band of 85 kDa. To determine which of the three known bombesin receptor subtypes (GRP receptor (GRP-R), neuromedin B receptor, bombesin receptor subtype-3) were expressed in the cell lines, reverse transcription/**PCR** analysis of cellular RNA followed by **hybridization** with receptor-specific cDNA was performed. This revealed the presence of GRP-R transcript in all cell lines, while neither of the other two receptor transcripts were expressed. When intracellular calcium mobilization was measured by Fura-2/AM cell labeling and spectrofluorometric monitoring, bombesin (100 nM) induced rapid calcium mobilization in both PC-3 (> 200% of baseline) and DU-145 (> 100% of baseline) cells, but not in LNCaP cells. However, as measured by 3-(4,5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide assay and

[3H]thymidine incorporation, no growth modulation was observed with bombesin or bombesin receptor antagonist at various concentrations (0-500 nM). Our data indicate that bombesin is a potent inducer of signal transduction via GRP-R receptors in androgen-insensitive PC-3 and DU-145 **prostate cancer** cells. This suggests that the bombesin/GRP family of neuropeptides may play a regulatory role in the biology of androgen-independent **prostate cancer**.

L31 ANSWER 37 OF 48 MEDLINE
96319801 Document Number: 96319801. Expression and processing of peptidylglycine alpha-amidating monooxygenase messenger RNA in rat prostate. Samos L F; Gkonos P J. (Geriatric Research, Education, and Clinical Center, Miami VA Medical Center, Florida, USA.) PROSTATE, (1996 Aug) 29 (2) 101-6. Journal code: PB4. ISSN: 0270-4137. Pub. country: United States. Language: English.

AB The prostate gland contains neuroendocrine cells and amidated neuroendocrine peptides whose presence has been related to aggressive forms of **prostate cancer**. The enzyme peptidylglycine alpha-amidating monooxygenase (PAM) is critical to the bio-synthesis of amidated peptides and is commonly present in neuroendocrine cells. By northern blot **hybridization** analysis, PAM mRNA was detected in similar quantities in dorsolateral and ventral prostates of 3-month-old and 13-month-old rats. Multiple forms of PAM mRNA were present whose size distribution was more similar to PAM mRNAs found in pituitary than atrium.

Alternative splice sites in PAM mRNA were investigated by reverse-transcriptase **polymerase chain reaction**. Similar alternatively spliced forms of PAM mRNA were found in both prostate lobes, pituitary, and atrium. However, the distribution of forms in the prostate most resembled that of pituitary. Multiple forms of PAM mRNA are present in prostate and may serve as markers of neuroendocrine differentiation.

L31 ANSWER 38 OF 48 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 5
1995:997463 Document No. 124:47617 Reverse transcriptase-**PCR** method for molecular staging of **prostate cancer** using PSA antigen mRNA. Katz, Aaron E.; Buttyan, Ralph; Raffo, Anthony; Olsson, Carl A. (Columbia University, USA). PCT Int. Appl. WO 9528498 A1 19951026, 92 pp. DESIGNATED STATES: W: AU, CA, JP, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1995-US4680 19950414. PRIORITY: US 1994-229391 19940415.

AB A method for enhancing the detection of prostate specific antigen in a biol. sample comprising (a) extg. mRNA from the sample; (b) contacting the mRNA from step (a) with reverse transcriptase under conditions allowing for the prodn. of cDNA; (c) contacting the cDNA from step (b) with a pair of reverse transcriptase **polymerase chain reaction** primers capable of specifically **hybridizing** with DNA encoding prostate specific antigen wherein one such primer is an **oligonucleotide** of 12 to 30 nucleotides in length and comprises the sequence 5-CACCCATCCTA-3' and wherein the second such primer is an **oligonucleotide** of 12 to 30 nucleotides in length and comprises the sequence 5'-TCCAGCCCACGAC-3'; and wherein at least one of the primers is covalently linked to a modified digoxigenin mol. and under conditions allowing for extension of the primers; and (d) detecting the resulting amplified DNA.

L31 ANSWER 39 OF 48 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 6
1996:62910 Document No.: PREV199698635045. Detection of prostate-specific

antigen mRNA by reverse transcription **polymerase chain reaction** and time-resolved fluorometry. Galvan, Barbara; Christopoulos, Theodore K. (1); Diamandis, Eleftherios P.. (1) Dep. Chem. Biochemistry, Univ. Windsor, 401 Sunset Ave. Windsor, ON N9B 3P4 Canada. Clinical Chemistry, (1995) Vol. 41, No. 12 PART 1, pp. 1705-1709. ISSN: 0009-9147. Language: English.

AB We have developed a time-resolved fluorometric **hybridization** assay for detecting prostate-specific antigen (PSA) mRNA amplified by reverse transcription **polymerase chain reaction**. During **PCR**, digoxigenin-11-dUTP is incorporated into the amplified product. An **oligonucleotide** internal to the primers is used as a specific probe, being biotinylated and captured on streptavidin-coated microtiter wells. Denatured **PCR** product **hybridizes** with the probe, and the **hybrids** are detected with an alkaline phosphatase-labeled antidigoxigenin antibody. We used the phosphate ester of fluorosalicylic acid as the substrate. The fluorosalicylate produced forms a highly fluorescent ternary complex with Tb-3+-EDTA, which we can measure by time-resolved fluorometry. A signal-to-background ratio of 10 was obtained when 160 PSA cDNA molecules were present in the preamplification sample. Also, mRNA corresponding to one LNCaP cell in the presence of 10-6 PSA-negative cells can be detected (signal-to-background ratio of 3.1). Samples containing 100, 1000, and 50 000 LNCaP cells gave CVs of 12.4%, 4.9%, and 6.8%, respectively (n = 10).

L31 ANSWER 40 OF 48 CAPLUS COPYRIGHT 2000 ACS

1995:725466 Document No. 123:140416 Growth of the androgen-dependent tumor of the prostate: role of androgens and of locally expressed growth modulatory factors. Limonta, Patrizia; Dondi, Donatella; Montagnani Marelli, Marina; Moretti, Roberta M.; Negri-Cesi, Paola; Motta, Marcella (Center for Endocrinological Oncology, University of Milano, Milan, 20133, Italy). J. Steroid Biochem. Mol. Biol., 53(1-6), 401-5 (English) 1995. CODEN: JSBBEZ. ISSN: 0960-0760.

AB A review, with 43 refs., on expts. performed to clarify: (1) the metab. of androgens in prostatic tumor cells; and (2) the role played by locally produced growth factors in the autocrine regulation of prostatic tumor cell proliferation and the possible regulation exerted by testosterone (T) on the activity of these factors. These studies have been performed by utilizing the human androgen-responsive prostatic cancer LNCaP cell line. By incubating LNCaP cells with different 14C-labeled androgenic precursors, it has been shown that all the major key enzymes involved in the metab. of androgens are present and active in these cells. In particular, the 5.alpha.-reductase, which converts T and androst-4-en-3,17-dione (.DELTA.4) to 17.beta.-hydroxy-5.alpha.-androstan-3-one (DHT) and 5.alpha.-androstan-3,17-dione (5.alpha.-A) resp., seems to be more active when .DELTA.4 is the substrate, suggesting a preference for this precursor. The hypothesis that LNCaP cells might produce LHRH (or a LHRH-like peptide) has been verified by RT-**PCR**, performed in the presence of a pair of specific **oligonucleotide** primers. A cDNA band of the expected size (228 bp), which specifically **hybridized** with a 32P-labeled LHRH **oligonucleotide** probe, has been obtained in LNCaP cells. To clarify the possible role played by this factor in the regulation of tumor growth, LNCaP cells, cultured in steroid-free

conditions, have been treated with a LHRH antagonist; the treatment resulted in a significant increase of cell proliferation. Taken together, these data indicate that LHRH (or LHRH-like) growth modulatory system is expressed in LNCaP cells and plays an inhibitory role in the regulation of tumor cell proliferation. This system seems to be regulated in a neg. way by steroids. Growth factors endowed with stimulatory activity, such as EGF and TGF.alpha., have also been shown to be produced by LNCaP cells. The present studies show that the immunopptn. of the EGF receptor with a specific monoclonal antibody (Ab225) reveals a protein band of the expected size (170 kDa) which is phosphorylated even in basal conditions. Moreover, the treatment of LNCaP cells, cultured in serum-free conditions, either with a monoclonal antibody against the EGF receptor, or with immunoneutralizing antibodies against EGF and TGF.alpha., results in a significant decrease of cell proliferation. These observations clearly confirm the expression, in prostatic tumor cells, of an EGF/TGF.alpha. loop which exerts a stimulatory action on cell proliferation. T seems to exert a pos. regulation on this loop, at least in terms of EGF receptor concn.

L31 ANSWER 41 OF 48 MEDLINE DUPLICATE 7

95340296 Document Number: 95340296. ras, p53 and HPV status in benign and malignant prostate tumors. Moyret-Lalle C; Marcais C; Jacquemier J; Moles J P; Daver A; Soret J Y; Jeanteur P; Ozturk M; Theillet C. (Institut de Genetique Moleculaire de Montpellier, France..) INTERNATIONAL JOURNAL OF CANCER, (1995 Apr 21) 64 (2) 124-9. Journal code: GQU. ISSN: 0020-7136. Pub. country: United States. Language: English.

AB To study the role of ras, p53 genes and HPV virus (16 and 18) in the development of **prostate cancer**, we analyzed tissue sections from 27 patients affected with carcinomas (stages A to D) and from 24 patients with adenomas. Mutations of H, K and N-ras and p53 (exons 2-9) were studied by SSCP and DNA sequencing. Accumulation of p53 protein was studied by immunohistochemistry on tissue sections. Tumors were also analyzed for the presence of HPV16 and -18 sequences by **PCR** and DNA **hybridization** with sequence-specific **oligonucleotides**. No mutation was found in the three ras genes studied, either in carcinomas or adenomas. By SSCP analysis we identified p53 mutations in only 2 of 19 carcinomas studied, both in exon 7. Immunohistochemical results strongly correlate with the SSCP results: p53 protein was positive in tumors with p53 mutation but not in others; 32% of studied adenomas had detectable HPV16 DNA, while 53% of carcinomas were HPV16+. Among these I presented a p53 mutation. No HPV18 E6 sequence could be detected. Our data show that in prostate tumors from France, mutations of p53 and ras are rare events but that these tumors display detectable HPV16 DNA at a high frequency. The low incidence of p53 mutation, associated to a significant proportion of tumors showing HPV16 DNA, could suggest that in **prostate cancer** HPV16 infection could participate in p53 inactivation by E6.

L31 ANSWER 42 OF 48 MEDLINE

95335662 Document Number: 95335662. Detection of eight BRCA1 mutations in 10 breast/ovarian cancer families, including 1 family with male breast cancer. Struewing J P; Brody L C; Erdos M R; Kase R G; Giambarresi T R; Smith S A; Collins F S; Tucker M A. (Genetic Epidemiology Branch, National

Cancer Institute, National Institutes of Health, Bethesda, MD 20892-7372, USA.) AMERICAN JOURNAL OF HUMAN GENETICS, (1995 Jul) 57 (1) 1-7.
Journal code: 3IM. ISSN: 0002-9297. Pub. country: United States. Language: English.

AB Genetic epidemiological evidence suggests that mutations in BRCA1 may be responsible for approximately one half of early onset familial breast cancer and the majority of familial breast/ovarian cancer. The recent cloning of BRCA1 allows for the direct detection of mutations, but the feasibility of presymptomatic screening for cancer susceptibility is unknown. We analyzed genomic DNA from one affected individual from each of 24 families with at least three cases of ovarian or breast cancer, using SSCP assays. Variant SSCP bands were subcloned and sequenced. Allele-specific **oligonucleotide hybridization** was used to verify sequence changes and to screen DNA from control individuals. Six frameshift and two missense mutations were detected in 10 different families. A frameshift mutation was detected in a male proband affected with both breast and **prostate cancer**. A 40-bp deletion was detected in a patient who developed intra-abdominal carcinomatosis 1 year after prophylactic oophorectomy. Mutations were detected throughout the gene, and only one was detected in more than a single family. These results provide further evidence that inherited breast and ovarian cancer can occur as a consequence of a wide array of BRCA1 mutations. These results suggests that development of a screening test for BRCA1 mutations will be technically challenging. The finding of a mutation in a family with male breast cancer, not previously thought to be related to BRCA1, also illustrates the potential difficulties of genetic counseling for individuals known to carry mutations.

L31 ANSWER 43 OF 48 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 8
1994:505540 Document No. 121:105540 Androgen-dependent prostatic tumors: biosynthesis and possible actions of LH-RH. Limonta, Patrizia; Moretti, Roberta M.; Dondi, Donatella; Marelli, Marina Montagnani; Motta, Marcella (Cent. Endocrinological Oncology, Univ. Milano, Milan, 20133, Italy). J. Steroid Biochem. Mol. Biol., 49(4-6), 347-50 (English) 1994. CODEN: JSBBEZ. ISSN: 0960-0760.

AB Testosterone (T) is the major exogeneous stimulus for the growth of prostatic carcinoma. It is believed that the proliferative action of T may be mediated by locally expressed growth modulatory factors. Recent evidence from the authors' lab. suggests that a LHRH (or a LHRH-like) loop might be expressed in human prostatic tumor cells. To verify this hypothesis, the authors have studied whether a mRNA for LHRH is expressed in the human androgen-responsive prostatic cancer cell line LNCaP, using the reverse transcription-**polymerase chain reaction** technique in the presence of a pair of specific **oligonucleotide** primers. A cDNA band of the expected size was obtained from LNCaP cells; this band **hybridized** with a 32P-labeled LHRH **oligonucleotide** probe and its sequence showed a complete match with the reported sequence of the human placental LHRH cDNA. These observations indicate that the mRNA coding for LHRH is expressed in LNCaP cells and suggest that a LHRH (or a LHRH-like) peptide might be produced by these cells. To clarify the possible action of this peptide, LNCaP cells were grown in a steroid-free medium and treated with a LHRH antagonist. The treatment resulted in a significant increase of tumor cell growth. These data clearly indicate that the LHRH system expressed in LNCaP cells plays an inhibitory role on cell proliferation, and that this system seems to be regulated in a neg. way by steroids. An EGF/TGF.alpha. autocrine stimulatory loop (peptides, receptors,

intracellular signals) is also functional in these cells. Treatment of LNCaP cells grown in serum-free conditions (i.e. in the absence of exogenous growth factors) with a monoclonal antibody against the EGF receptor, or with immunoneutralizing antibodies against EGF or TGF.alpha., resulted in a significant decrease of cell proliferation. T pos. regulates this EGF/TGF.alpha. system by increasing the concn. of eGF binding sites. The present data indicate that an inhibitory LHRH (or LHRH-like) system is expressed in LNCaP cells and participates in the local mechanisms regulating tumor cell proliferation together with an EGF/TGF.alpha. stimulatory loop. Both systems appear to be modulated by T.

L31 ANSWER 44 OF 48 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 9
1993:469202 Document No. 119:69202 Expression of luteinizing hormone-releasing hormone mRNA in the human prostatic cancer cell line LNCaP. Limonta, Patrizia; Dondi, Donatella; Moretti, Roberta M.; Fermo, Daniela; Garattini, Enrico; Motta, Marcella (Dep. Endocrinol., Univ. Milano, Milano, 20133, Italy). J. Clin. Endocrinol. Metab., 76(3), 797-800 (English) 1993. CODEN: JCEMAZ. ISSN: 0021-972X.
AB LHRH or a LHRH-like peptide might be produced by human prostatic tumor cells. The LHRH mRNA expression in the human prostatic cancer cell line LNCaP was studied by the reverse transcription-**polymerase chain reaction** (RT-**PCR**) technique. The mRNA was extd. from LNCaP cells, rat brain hypothalamus, and rat pituitary gland, was reverse transcribed to cDNA, and amplified by **PCR** utilizing a pair of **oligonucleotide** primers complementary to the LHRH cDNA. Following gel electrophoresis, a band of the expected size of 228 base pairs was found in LNCaP cells as well as in the rat hypothalamus, but not in the rat anterior pituitary. The bands from the LNCaP cells and rat hypothalamus specifically **hybridized** to a 32P-labeled LHRH **oligonucleotide** probe. The cDNA band obtained from LNCaP cells was subcloned into a plasmid vector, and the anal. of its sequence showed a complete match with the authentic human placental LHRH cDNA. Thus, LHRH mRNA is expressed in human prostatic cancer cells and LHRH or a LHRH-like peptide may be produced by these cells. This material might act as a local growth regulating factor on tumor cell proliferation. LNCaP cells, grown in a steroid-free medium, were treated daily with a potent LHRH antagonist. After 9, 12, and 15 days, the treatment increased the tumor cell proliferation. LHRH mRNA expressed in LNCaP cells is possibly translated into LHRH or a LHRH-like peptide which may function as a local growth inhibitory factor on the prostatic tumor cell proliferation by acting on LHRH receptors.

L31 ANSWER 45 OF 48 MEDLINE DUPLICATE 10
93205621 Document Number: 93205621. Detection of human papillomavirus (HPV) DNA in human prostatic tissues by **polymerase chain reaction (PCR)**. Sarkar F H; Sakr W A; Li Y W; Sreepathi P; Crissman J D. (Department of Pathology, Wayne State University School of Medicine, Detroit, Michigan 48201..) PROSTATE, (1993) 22 (2) 171-80. Journal code: PB4. ISSN: 0270-4137. Pub. country: United States. Language: English.
AB Human papillomavirus (HPV) infections are strongly linked to the pathogenesis of uterine cervical neoplasms, and have been implicated in

other cancers of the female genital tract. In contrast, the association of HPV with the cancers of the male urogenital tract is less evident, except in anal and penile cancers. However, recent studies reporting the prevalence of HPV infections in human **prostate cancers** (60-100% HPV 16 positive vs. no infection of HPV) have raised controversies regarding the prevalence of HPV in benign and neoplastic human prostate. We investigated the prevalence of HPV infections in prostatic intraepithelial neoplasia (PIN) and prostatic adenocarcinomas in 23 surgically resected prostates. **Polymerase chain reaction** (**PCR**) was used to amplify HPV 6b/11, 16, and 18 specific DNA sequences, using type specific HPV primers selected from the transforming gene E6-E7. The areas of PIN and cancer in 6 microns H&E stained tissue sections were identified, and respective areas of PIN and cancer were isolated from the adjacent serial sections and used for DNA amplification and HPV detection (Fig. 1). Our results demonstrated the presence of HPV 16 in three carcinomas (13%), using type specific primers in **PCR** amplified samples. We were not able to demonstrate the presence of other HPV types (HPV 6b/11 or HPV 18) in any of the samples using specific primers. Two of these prostates showed relatively strong positive signals by dot blot analysis, when **hybridized** with a 32P-labeled HPV 16 type specific **oligonucleotide** probe. One more sample showed weak positivity, when **hybridized** with a 32P-labeled HPV 16 type specific **oligonucleotide** probe. Subsequently, we have confirmed these results by Southern **hybridization** of the samples transferred to nylon membrane after agarose gel electrophoresis and detected by HPV 16 type specific **oligonucleotide** probe, using chemiluminescent assay. We, therefore, conclude that HPV infections of the prostate in general are not as common as has been previously claimed by other investigators.

L31 ANSWER 46 OF 48 CAPLUS COPYRIGHT 2000 ACS
1994:130973 Document No. 120:130973 ras Gene mutations of human prostate carcinoma. Watanabe, Masatoshi (Sch. Med., Mie Univ., Tsu, 514, Japan). Mie Med. J., 43(1), 87-95 (English) 1993. CODEN: MMJJAI. ISSN: 0026-3532.

AB Twenty-one latent prostate carcinomas and twenty-three clin. prostate carcinomas were studied for ras gene mutations by mutation-specific **oligonucleotide** probe **hybridization** after **polymerase chain reaction** (**PCR**) amplification. Nine of the 44 (20%) contained ras gene mutations, a significantly higher frequency than has been reported in the United States. Five of the 21 latent prostate carcinomas contained ras gene mutations: three at codon 12 of K-ras had GGT to GTT transversions, and two at codon 12 of N-ras and had GGT to AGT transition. Four of the 23 clin. prostate carcinomas contained ras gene mutations: two at codon 61 of N-ras and these had CAA to CTA transversion, another at codon 12 of K-ras and had a GGT to GTT transversion, and the other at codon 61 of H-ras and had a CAG to CTG transversion. The presence of ras mutation did not correlate with age nor with histol. findings. There was a difference in the frequency of ras gene mutations between latent carcinoma and clin. carcinoma. These observations indicate the possibility that ras gene mutations are characteristic of the initial stage of carcinogenesis of the prostate glands.

L31 ANSWER 47 OF 48 MEDLINE DUPLICATE 11
92302101 Document Number: 92302101. Infrequent RAS oncogene mutations in

human **prostate cancer**. Moul J W; Friedrichs P A; Lance R S; Theune S M; Chang E H. (Department of Surgery Uniformed Services, University of the Health Sciences, Bethesda, MD 20814-4799..) PROSTATE, (1992) 20 (4) 327-38. Journal code: PB4. ISSN: 0270-4137. Pub. country: United States. Language: English.

AB The RAS gene family includes three functional genes, H-RAS, K-RAS, and N-RAS, which have been most widely studied in human tumors. Point mutations most commonly occurring at codons 12, 13, or 61 of these genes allow the RAS protooncogene to be converted to a RAS oncogene. A variety of human tumors have been studied for RAS mutations to date, however, conflicting data has been reported regarding **prostate cancer**. Cell line studies and two American studies of clinical material have found a low incidence of RAS mutation in **prostate cancer**. The few mutations found were predominantly in the H-RAS gene. Conversely, a recent study of Japanese occult autopsy specimens found an approximate 25% incidence of K-RAS mutations. In this current study, DNA was extracted from 24 archival paraffin-embedded, formalin-fixed radical prostatectomy specimens. Twenty-one of the 24 cases had pathologic stage C disease, and paraffin blocks were selected having the most concentrated area of neoplasm. Twelve, seven, and five cases demonstrated moderate, well and poorly differentiated histologic grade respectively. **Polymerase chain reaction** (**PCR**) was used to amplify the K-RAS, N-RAS, and H-RAS 12, 13, 61 codons of these specimens and mutations were detected with mutation-specific **oligonucleotide** probe **hybridization** of southern and slot blots. No definite point mutations were detected. **PCR**'s and **hybridizations** were performed three separate times by three investigators to confirm these results. **PCR** -generated mutation-specific positive controls and known negative controls were used and found to be important to interpret **oligonucleotide hybridization** assays. RAS gene mutations appear to be infrequent in clinical prostate carcinomas in American males.

L31 ANSWER 48 OF 48 CAPLUS COPYRIGHT 2000 ACS

1993:487398 Document No. 119:87398 Detection of human papillomavirus (HPV) DNA in human prostatic tissues by **polymerase chain reaction (PCR)**. Sarkar, Fazlul H.; Sakr, Wael A.; Li, Yi Wei; Sreepathi, Prabhakar; Crissman, John D. (Sch. Med., Wayne State Univ., Detroit, MI, 48201, USA). Prostate (N. Y.), 22(2), 171-80 (English) 1992. CODEN: PRSTDS. ISSN: 0270-4137.

AB Human papillomavirus (HPV) infections are strongly linked to the pathogenesis of uterine cervical neoplasms, and have been implicated in other cancers of the female genital tract. In contrast, the assocn. of HPV with the cancers of the male urogenital tract is less evident, except in anal and penile cancers. However, recent studies reporting the prevalence of HPV infections in human **prostate cancers** (60-100% HPV 16 pos. vs. no infection of HPV) have raised controversies regarding the prevalence of HPV in benign and neoplastic human prostate. The prevalence of HPV infections in prostatic intraepithelial neoplasia (PIN) and prostatic adenocarcinomas was studied in 23 surgically resected prostates. **Polymerase chain reaction** (**PCR**) was used to amplify HPV 6b/11, 16, and 18 specific DNA sequences, using type-specific HPV primers selected from the transforming gene E6-E7. The areas of PIN and cancer in 6 .mu.m H&E stained tissue sections were identified, and resp. areas of PIN and cancer were isolated from the adjacent serial sections and used for DNA amplification and HPV detection. The results demonstrated the presence of HPV 16 in 3 carcinomas (13%), using type-specific primers in **PCR**-amplified samples. The authors were not able to demonstrate the presence of other

HPV types (HPV 6b/11 or HPV 18) in any of the samples using specific primers. Two of these prostates showed relatively strong pos. signals by dot blot anal., when **hybridized** with a 32P-labeled HPV 16 type-specific **oligonucleotide** probe. One more sample showed weak positivity, when **hybridized** with a 32P-labeled HPV 16-type-specific **oligonucleotide** probe. These results were confirmed by Southern **hybridization** of the samples transferred to nylon membrane after agarose gel electrophoresis and detected by HPV 16 type-specific **oligonucleotide** probe, using chemiluminescent assay. Thus, HPV infections of the prostate in general are not as common as has been previously claimed by other investigators.

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'IN' IS NOT A VALID FIELD CODE
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L33       6643 FILE CAPLUS
L34       1905 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L35        981 FILE EMBASE
L36        503 FILE WPIDS

TOTAL FOR ALL FILES
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'IN' IS NOT A VALID FIELD CODE
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L46         10 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L47          5 FILE EMBASE
L48          4 FILE WPIDS

TOTAL FOR ALL FILES
L49         40 MITCHAM J?/AU,IN

=> s l37 and l43 and l49

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L51          1 FILE CAPLUS
L52          0 FILE BIOSIS
L53          0 FILE EMBASE
L54          1 FILE WPIDS

TOTAL FOR ALL FILES
L55          2 L37 AND L43 AND L49
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